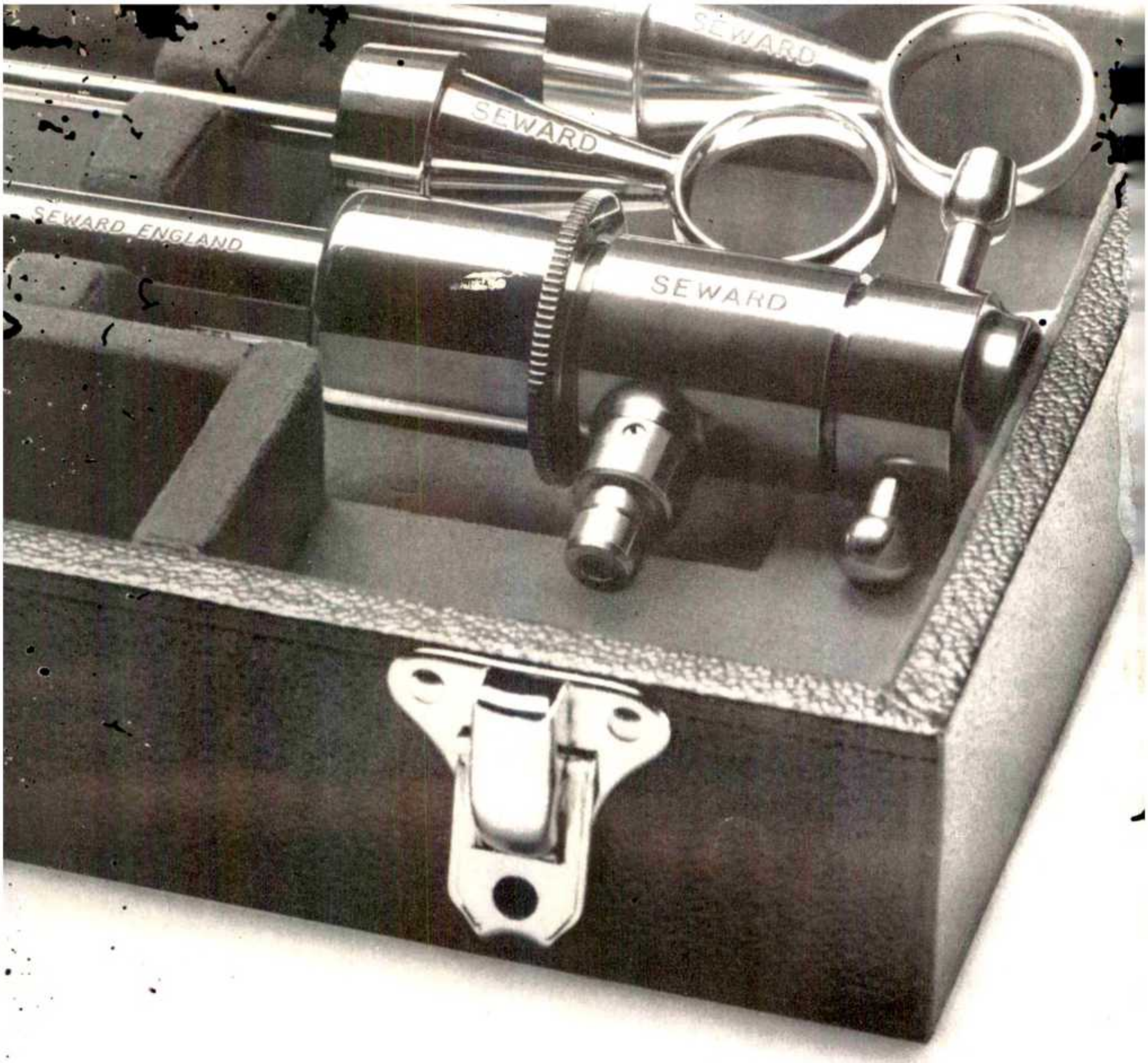


The Seward Identikit...

Every stainless steel Lloyd-Davies' Sigmoidoscope made by Seward has components which are absolutely identical – guaranteed interchangeable.

And that's an immense advantage when a lot of these instruments pass through the CSSD together. Because you never need to label any parts, or worry about 'matching up'.

Which saves time. Cuts losses.

You'll probably agree, the Seward Lloyd-Davies' Sigmoidoscope* is good news.

Well, here's some more.

The Seward St. Mark's Proctoscope*.

Made entirely of stainless steel. With all parts absolutely identical – guaranteed interchangeable.

**Electric and non-electric models available – leaflets on request*

seward –the fast word in quality

A. J. Seward, UAC House, Blackfriars Road, London SE1 9UG.
Telephone: 01-928 7444

P 25,354

CVK-A06337-5-P25,354

Vol. 62 : No. 1 : January 1975

The British Journal of Surgery

5

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
H. A. F. DUDLEY London (Surgical Research Society)
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN MCADAM Kampala : Uganda
A. C. MCEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL J. WATT Naval Medical Service
*R. B. WELBOURNE London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

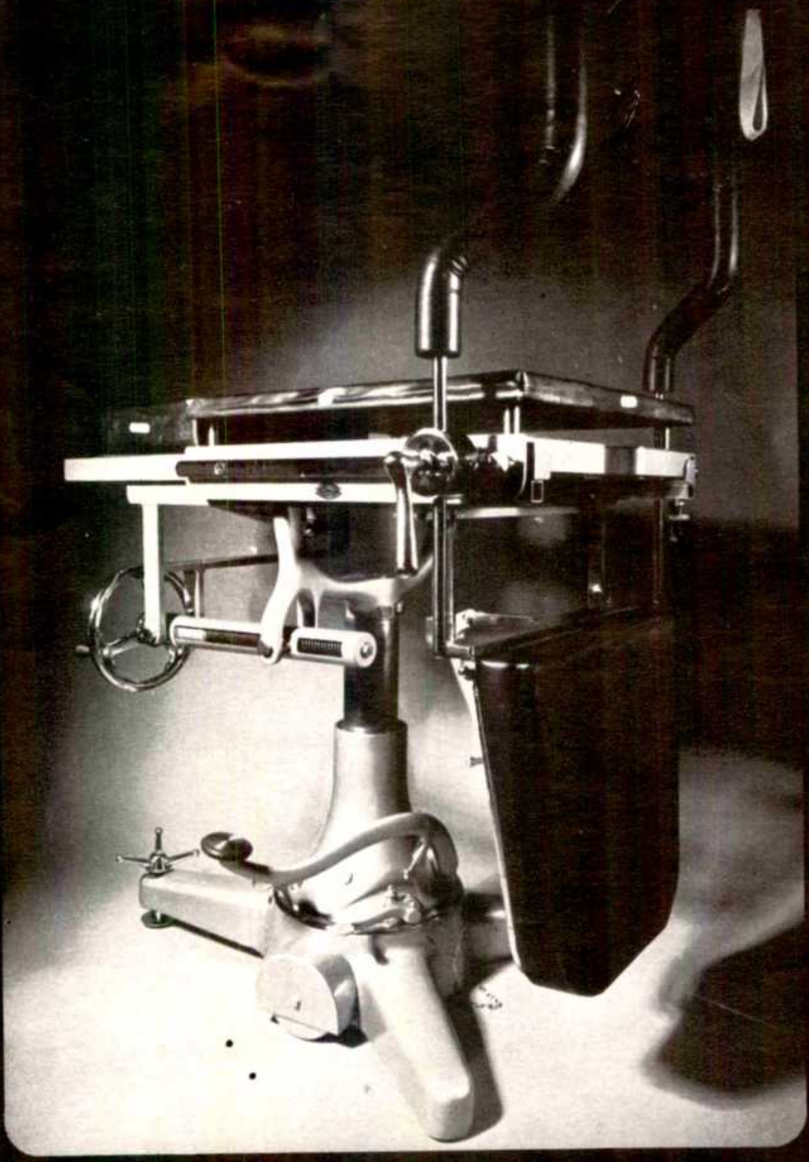
* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX

Subscription £15 per annum, post free. Single copies £1·50, post free

THE WILLIAMS & WILKINS CO., BALTIMORE
Second Class Postage paid at Baltimore, and at additional mailing offices.

THACKRAY



Belfast table

A table for perineal and general surgery which is designed to allow the patient to be placed in lithotomy position without being lifted or pulled down the table.

Chas. F. Thackray Limited, Head Office: P.O. Box 171 Park Street, Leeds LS1 1RQ.

The British Journal of Surgery

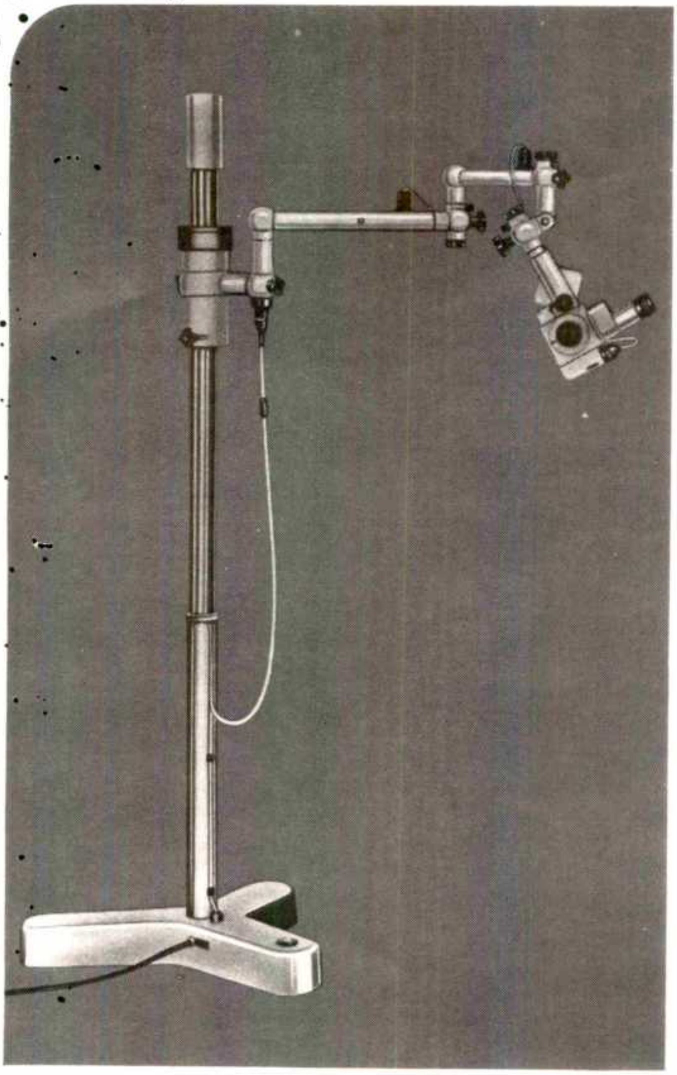
Vol. 62 : No. 1 : January 1975

Original papers

		Page
Long survival after operation for cancer of the lung	Lord Brock	1
Fatal cardiac tamponade and other mechanical complications of central venous catheters	T. E. B. Dane and E. G. King	6
The response of the lower oesophageal sphincter to maximal doses of pentagastrin	L. M. Trindade, I. L. Rosenberg, Z. J. Rozycki and G. R. Giles	11
Relationship between changes in plasma gastrin and lower oesophageal sphincter pressure after meals	I. W. McCall, R. F. Harvey, Caroline J. Owens and B. G. Clendinnen	15
A survey of the results of the Boerema anterior gastropexy for hiatus hernia over a 4-year period	C. J. Davies	19
Atrophic gastritis in gastrectomy specimens	J. M. Skinner, P. J. Heenan and R. Whitehead	23
A clinicopathological review of 68 carcinomas of the gallbladder	L. A. Donaldson and A. Busuttil	26
Primary carcinoma of the gallbladder	A. T. M. Prakash, Lalit K. Sharma and P. N. Pandit	33
The natural and unnatural history of pancreatic pseudocysts	S. Sankaran and Alexander J. Walt	37
The occult osteomatous changes in the mandible in patients with familial polyposis coli	Joji Utsunomiya and Tadashi Nakamura	45
The continent ileostomy of Kock (ileal intra-abdominal reservoir)	Jan F. Halvorsen and Peter Heimann	52
Torsion of the testis: a review of 22 cases	M. G. Greaney	57
Surgical sterilization by vasectomy and its effect on the structure and function of the testis in man	A. S. Gupta, L. K. Kothari, A. Dhruva and R. Bapna	59
The relationship between ultrasound assessment and angiography in occlusive arterial disease of the lower limb	J. Chamberlain, E. Housley and A. I. S. Macpherson	64
Phenol sympathectomy in the treatment of intermittent claudication: a controlled clinical trial	T. Fyfe and R. O. Quin	68
A clinical trial designed to discover if the primary treatment of varicose veins should be by Fegan's method or by an operation	F. S. A. Doran and Mary White	72
Secondary involvement of the penis by rectal cancer	B. I. Rees	77

Reviews and notices of books 80

© John Wright & Sons Ltd and the respective contributors named above, 1975.
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.



SURGERY MICROSCOPE II

Another superb instrument from

CARL ZEISS
JENA

This well established Surgery Microscope from VEB Carl Zeiss Jena has gained a well deserved reputation for it's reliability and all-round performance. It is extremely versatile, allowing complete freedom of movement. The working distance is 200-300 or 400mm. You'll be surprised at the competitive price of this popular microscope which incorporates optics of the highest quality. Remarkable value!

SPECIAL FEATURES INCLUDE:-

- ✻ Individually focussing eyepieces
- ✻ Rapid changing for two filters and five magnifications (5x, 8x, 12.5x, 20x, 32x)
- ✻ Observer eyepiece available
- ✻ Photographic attachments available.

Write or telephone for literature or demonstration on this instrument and others in the comprehensive VEB Carl Zeiss Jena Range.

CARL ZEISS JENA LTD., C.Z. Scientific Instruments Ltd.,
P.O. Box 43, 2 Elstree Way, Borehamwood, Herts WD6 1NH. *Tel: 01-953 1688.*
Manufactured by: VEB Carl Zeiss Jena, Carl Zeiss Strasse 1, Jena, GDR.

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 60. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are two or more authors (apart from the main author), these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title

of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature (Lond.)* **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea **4**, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th ed. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology.* London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BEAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

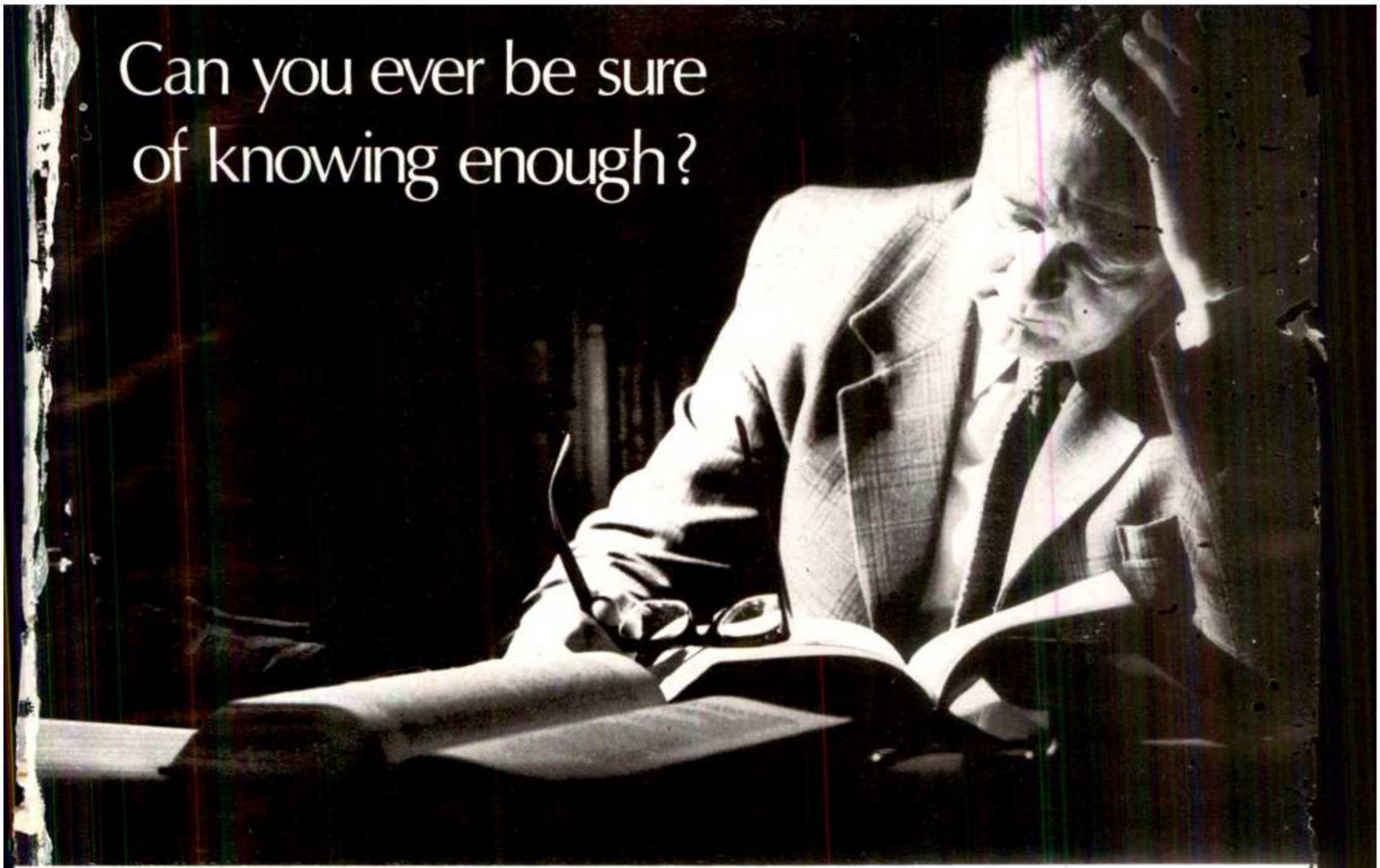
Congress Proceedings

CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding, or that following.,

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)


Can you ever be sure
of knowing enough?

THE SCIENTIFIC FUNDAMENTALS OF SURGERY

By: **J. GWYNNE BROCKIS, Ch.M. (Leeds), FRCS (Eng), FRACS.** *Associate Professor of Surgery, University of Western Australia; Surgeon to Royal Perth and Sir Charles Gairdner Hospitals, Perth, Western Australia.*

730 pp. Ill. £10.00 0 407 39000 6

A thorough and comprehensive presentation of the basic sciences on which the surgeon's decision is based. The text has been prepared with special regard to the needs of doctors studying for the Fellowship Examination of the Royal College of Surgeons of England.

SPINAL DYSRAPHISM: Spina Bifida Occulta

By: **C.C. MICHAEL JAMES, Ph.D. (Ed), FRCS (Edin).** *Orthopaedic Surgeon, W.J. Sanderson Orthopaedic Hospital, Newcastle upon Tyne and Newcastle General Hospital; Clinical Lecturer in the University of Newcastle upon Tyne. and*

L.P. LASSMAN, MB, BS(Lond), FRCS.
Neurological Surgeon, Regional Neurological Centre, Newcastle General Hospital and Royal Victoria Infirmary, Newcastle upon Tyne, Clinical Lecturer in the University of Newcastle upon Tyne.

152 pp. Ill. £4.40 0 407 39870 8

An account of 100 cases of spina bifida occulta submitted to laminectomy by two pioneers in the field.

SURGERY OF THE LUNG – The Coventry Conference

Ed. by **R.E. SMITH, MA, MB, BChir, FRCP.** *Area Director of Postgraduate Medical Education, Warwickshire, and*

W.G. WILLIAMS, MA, MChir, FRCS. *Consultant Thoracic Surgeon, Walsgrave Hospital, Coventry.*

276 pp. Ill. £6.50 0 407 40130 X

This book contains the proceedings of a conference held in Coventry in 1973, which brought together the experience of distinguished international experts in the field of lung surgery.

SURGERY OF THE OESOPHAGUS– The Coventry Conference

Ed.by: **R. ABBEY SMITH, ChM, FRCS, FRCS (Ed).**
Consultant Thoracic Surgeon South Worcestershire, South Warwickshire, Coventry and Burton Hospital Groups, and

R.E. SMITH, MA, BChir, FRCP. *Area Director of Postgraduate Medical Education, Warwickshire.*

258 pp. Ill. £6.00 0 407 40150 4

Proceedings of a conference held in Coventry at which leading thoracic surgeons from all parts of the world discussed recent advances in oesophageal surgery.

SURGICAL DEPARTMENTS IN HOSPITALS– The Surgeon's View

Ed.by: **PROFESSOR SIR DONALD M. DOUGLAS, MBE, MB, ChM, MS (Minn), FRCS, FRCS (Ed).** *Professor of Surgery, University of Dundee, President of the Royal College of Surgeons of Edinburgh.*

144pp. Ill. £2.50 0 407 40340 X

The findings of a Study Group set up in 1967 to report on the planning and organization of surgical departments in hospitals. This makes absorbing reading for all surgeons, theatre nurses and hospital administrators, and is invaluable to hospital specialists engaged in planning new departments.

A SYSTEM OF ORTHOPAEDICS AND FRACTURES–4th Edition

By: **A. GRAHAM APLEY, MB, BS, FRCS.**
Consultant Orthopaedic Surgeon, Rowley Bristow Orthopaedic Hospital, Pyrford, Surrey; Consultant in Administrative Charge of the Accident and Emergency Centre, St.Peter's Hospital, Chertsey, Surrey.

284 pp. Ill. £7.50 0 407 30705 2

This book is a must for the postgraduate student reflecting, as it does, the important changes in the subject during the past few years and with the text and illustrations extensively updated. For surgeons and all those engaged in the care and management of orthopaedic and fracture patients this is an essential book.

THE UPPER CERVICAL SPINE
Regional Anatomy, Pathology and Traumatology
A Systematic Radiological Atlas and Text Book

By: **DETLEF VON TORKLUS,** *Senior Lecturer in Orthopaedic Surgery, University of Hamburg; Director, Orthopaedic Clinic and Outpatient Department, University Hospital, Hamburg, and*

WALTER GEHLE, *Lecturer and Clinical Tutor in Orthopaedic Surgery, University of Hamburg; Senior Staff Physician, Orthopaedic Clinic and Outpatient Department, University Hospital, Hamburg.*

English Translation by L.S. Michaelis, MD.

112 pp. Ill. £7.00 0 407 91001 8

A thorough account of the anatomy and pathology of the upper cervical spine with comment on related clinical symptoms. The authors' original findings will be of considerable interest to radiologists, orthopaedic surgeons and physicians, neurologists and neurosurgeons.

WESTMINSTER HOSPITAL SYMPOSIUM ON CHRONIC DUODENAL ULCER

Ed.by: **CHRISTOPHER WASTELL, MS, FRCS.** *Senior Lecturer in Surgery, Westminster Hospital Medical School; Honorary Consultant Surgeon, Westminster Hospital, London.*

283 pp. Ill. £5.00 0 407 10001 6

The proceedings of the Symposium held at Westminster Hospital Medical School on 24th–25th May, 1973, which attracted an important team of speakers, each well known for his specific subject.

POSTGRADUATE SURGERY LECTURES 2

Ed.by: **JOHN McFARLAND, MD, ChM, FRCS.**
1974. 132 pp. Ill. £2.65. 0 407 10006 7.

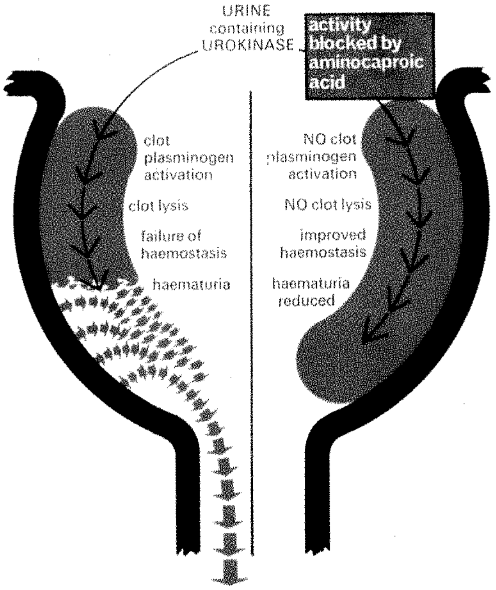
This second volume in the Postgraduate Surgery Lectures series presents selected lectures from the 1972–73 season at the Liverpool Medical Institution.

Turn another page of experience and knowledge with

THE BUTTERWORTH GROUP

88 Kingsway, London, WC2B 6AB. Telephone: 01-405-6900 and
Borough Green, Sevenoaks, Kent, TN15 8PH. Telephone: 0732–884507

The mechanism of post-prostatectomy bleeding and EPSIKAPRON® control



Epsikapron (aminocaproic acid) is rapidly excreted in the urine in high concentration ; there it inhibits urokinase, the fibrinolytic enzyme in urine. With the haemorrhage-sustaining property of urine blocked, the haemostatic coagulum becomes adequate, and blood loss is diminished substantially.

Epsikapron makes your prostatectomy patient's post-operative course smoother by diminishing :

the need for post-operative blood transfusion
clot retention
catheterization
the risk of infection
the period of hospitalization

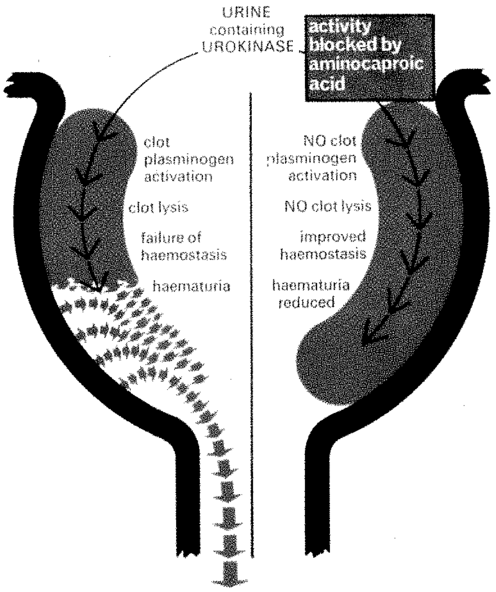
Presentation
Epsikapron Solution for Injection 0.4 g/ml Box of 6 ampoules of 10 ml, each containing 4.0g aminocaproic acid (0022/5003) Epsikapron Effervescent Powder 50% Box of 30 sachets, each containing 3.0g aminocaproic acid (0022/5004) Epsikapron Syrup 0.3g/ml Bottle of 250ml (0022/5005)

EPSIKAPRON®

KABI

Manufacturer : AB Kabi, Stockholm, Sweden.
Further information from:
Kabi Pharmaceuticals Ltd,
Bilton House, Uxbridge Road, Ealing, London W5 2TH.
Telephone : 01-567 4717 or 01-579 1871.

The mechanism of post-prostatectomy bleeding and EPSIKAPRON® control


URINE containing UROKINASE
activity blocked by aminocaproic acid
clot plasminogen activation
clot lysis
failure of haemostasis
haematuria
NO clot plasminogen activation
NO clot lysis
improved haemostasis
haematuria reduced

Epsikapron (aminocaproic acid) is rapidly excreted in the urine in high concentration; there it inhibits urokinase, the fibrinolytic enzyme in urine. With the haemorrhage-sustaining property of urine blocked, the haemostatic coagulum becomes adequate, and blood loss is diminished substantially.

Epsikapron makes your prostatectomy patient's post-operative course smoother by diminishing:

the need for post-operative blood transfusion
clot retention
catheterization
the risk of infection
the period of hospitalization

Presentation
Epsikapron Solution for Injection 0.4 g/ml Box of 6 ampoules of 10 ml, each containing 4.0g aminocaproic acid (0022/5003) Epsikapron Effervescent Powder 50% Box of 30 sachets, each containing 3.0g aminocaproic acid (0022/5004) Epsikapron Syrup 0.3g/ml Bottle of 250ml (0022/5005)

EPSIKAPRON®

KABI

Manufacturer: AB Kabi, Stockholm, Sweden.
Further information from:
Kabi Pharmaceuticals Ltd,
Bilton House, Uxbridge Road, Ealing, London W5 2TH.
Telephone: 01-567 4717 or 01-579 1871.

Table I: RESULTS OF LOBECTOMY IN 86 CASES

	No. of cases
Died from operation	3 (3·5%)
Died since operation	73
Still alive	10

Table II: LONG TERM SURVIVAL AFTER LOBECTOMY

Survival (yr)	No. of cases
5+	18
10+	12
16+	2
21	1
29	1

Table III: RESULTS OF SIMPLE PNEUMONECTOMY IN 89 CASES

	No. of cases
Died from operation	17 (20%)
Died since operation	70
Still alive	2

Table IV: LONG TERM SURVIVAL AFTER SIMPLE PNEUMONECTOMY

Survival (yr)	No. of cases
5+	2
6–10	3
11–15	6
16–20	3
21–30	5
Still alive after 30 yr	1
Still alive after 34 yr	1

Table V: RESULTS OF RADICAL PNEUMONECTOMY IN 118 CASES

	No. of cases
Died from operation	18 (15·25%)
Died since operation	89
Still alive	11

Table VI: LONG TERM SURVIVAL AFTER RADICAL PNEUMONECTOMY

Survival (yr)	No. of cases
5+	1
6–10	16
11–15	13
16–20	5
21–25	4

Table VII: COMPARATIVE RESULTS IN 293 CASES

Operation	Total no. of cases	Mortality (%)	5-year survival (%)	Still alive
Lobectomy	86	3·50	41	10
Simple pneumonectomy	89	30·00	30	2
Radical pneumonectomy	118	15·25	39	11
Total	293	13·00	32	23

in 86 (somewhat less than one-third). Any procedure that can combine removal of the growth with conservation of functioning lung tissue is preferable. It is repellent to excise a quantity of healthy lung that could with advantage have been left.

On the other hand, by being too conservative surgeons can endanger the chance of their patient being cured. The first aim with this dreadful disease should be to cure the patient. It is long survival that counts, especially in the many patients aged 40 or 50 presenting with this disease. A weak policy of conservatism routinely is surely not in the best interests of the patient. Cancer of the lung is not a standard disease and the type of operation to be done should be decided by a survey of each individual problem.

For example, an elderly patient with a well-localized tumour within a lobe can be treated by lobectomy. When respiratory function is impaired it becomes important to conserve lung tissue at any age. However, for a man of less than 50 years of age the chance of a lasting cure and of longevity is paramount and in general this demands a more radical operation. This is in keeping with our knowledge of cancer anywhere in the body. When some form of biological control becomes possible no doubt we shall be able to profit by planning less radical types of operation for cancer. At present a subradical course of treatment with radiotherapy can be a valuable preliminary to operation, as has been shown by results with and without this adjuvant. So far cytotoxic drug therapy has not been helpful.

Pneumonectomy, as ordinarily practised, might well be thought a radical procedure in itself. Indeed it may be a fully radical procedure, but it cannot be so in all cases. The classic cancer operations demand removal of the affected viscus together with its fascial connections and as much of the associated lymphatic field as possible. A more radical operation will include removal of the anterior and posterior mediastinal fatty tissue and lymph nodes, and clearance of the right or left tracheobronchial group of nodes and also most of the inferior tracheobronchial group. It is also important to secure as a routine the vessels within the pericardium and to excise an area of pericardium around the main vessels in order to avoid disturbing the hilar structures, especially the lymphatics. Details of the radical operation are available in the original description of the operation (Brock and Whytehead, 1955).

This more radical operation does not carry a higher mortality as the results will show. A radical procedure permits removal of the lung in a higher proportion of cases and thus the range of operability is increased. Although this inevitably embraces more poor risk subjects the mortality is still not adversely affected.

Results

Lobectomy

Table I shows the results of lobectomy in 86 cases. *Table II* shows the long term survival after operation. It will be seen that 2 patients survived for more than 20 years; one is still alive after 29 years and had a second lobectomy (contralateral) 13 years ago. Thus 34 patients lived 5 years or more; that is 40 per cent of those who had an operation and 41 per cent of those who survived operation.

Simple pneumonectomy

Table III shows the figures for this operation. *Table IV* shows the long term survival after operation. It will be seen that 8 patients survived for over 20 years and 2 for over 30 years. Both the latter patients are still alive at 30 and 34 years. Thus 21 patients lived

Br. J. Surg. Vol. 62 (1975) 6–10

Fatal cardiac tamponade and other mechanical complications of central venous catheters

T. E. B. DANE AND E. G. KING*

SUMMARY

A fatal cardiac tamponade caused by an intact polyethylene central venous catheter perforating the wall of the right ventricle is reported. A retrospective review of 105 central venous catheters used in an intensive care unit revealed a high incidence of catheter malposition and a 20 per cent mechanical complication rate. The possible causes of these malpositions and complications are discussed. Guidelines for the safer use of central venous catheters are presented.

A POLYETHYLENE central venous catheter caused fatal cardiac tamponade by perforating the right ventricular wall of a 70-year-old man. This accident prompted a retrospective review of catheter location and mechanical complications in a series of 105 central venous catheters. The findings from this review have been used to formulate guidelines for the safer use of these catheters.

Case report

A 70-year-old white male required intensive care following surgery for a complicated strangulated inguinal hernia. His problems included hypovolaemia, abdominal sepsis, oliguria and hypoxaemic respiratory failure. A 95-cm polyethylene catheter (Argyle Medicut) was inserted in his left antecubital fossa by surgical cutdown on the basilic vein. Its position in the superior vena cava with the tip entering the right antrium was confirmed radiologically. This catheter was used to monitor central venous pressure, to draw venous blood samples and to infuse intravenous fluids.

The patient's condition improved initially, but he needed a repeat laparotomy to repair a leak from the bowel anastomosis, tracheostomy for prolonged ventilatory support and haemodialysis for acute renal failure. On the twelfth day in hospital a similar polyethylene catheter was inserted in his right antecubital fossa by surgical cutdown on the basilic vein. It was also shown radiologically to be located in the superior vena cava with its tip entering the right atrium. This catheter was used without incident for 24 days to infuse casein protein hydrolysate (C.P.H., Cutter Laboratories), 50 per cent dextrose solution and fat emulsion (Intralipid 10 per cent, Pharmacia) with an infusion pump at a total volume of 120 ml/hour.

At 16.30 hours on day 36 the catheter in the patient's right arm began to leak from a crack in the exposed portion and was replaced by a similar catheter inserted at the same site. Radiological location of the new catheter showed it to be too far advanced and coiled in the right atrium and superior vena cava (*Fig.* 1). The catheter was withdrawn 12·5 cm but a repeat X-ray to confirm its position was not done. Infusion of the intravenous feeding solutions was continued as before and the patient remained well until 16.00 hours on day 38. He then became restless and nauseated, a nasogastric tube was inserted and he remained well until 18.00 hours that day, when he again became restless and nauseated. His vital signs remained stable throughout this period. Fifteen minutes later, while being examined to determine the cause for his restlessness, he developed a bradycardia of 40/minute, lost consciousness and had no recordable blood pressure. Cardiopulmonary resuscitation was started immediately but the bradycardia progressed to asystole which was unresponsive to all attempts to reverse it. While attempting to insert a transthoracic pacing electrode 15 minutes after starting resuscitation, a white liquid was aspirated from the region of the heart. Approximately 100 ml of this white material were removed but resuscitation was still unsuccessful. The central venous catheters were left *in situ* until post-mortem examination was carried out.

At post-mortem the anterior mediastinum and left pleural space contained a small amount of the white liquid and 80 ml were aspirated from the pericardial sac. This liquid was macroscopically similar to the intravenous feeding mixture being infused prior to the patient's death. When the pericardium was opened, the tip of a polyethylene catheter was found to be protruding 1 cm from the anterior surface of the right ventricle. There was an area of bruising, approximately 2 cm in diameter, on the surface of the myocardium around the catheter exit site (*Fig.* 2). Opening the heart revealed that the catheter from the left arm ended in the right atrium, but the other, from the right arm, crossed the tricuspid valve and perforated the anterior wall of the right ventricle (*Fig.* 3).

Review of central venous catheter locations and complications

The records and X-rays of all patients admitted to an 8-bed surgical intensive care unit over a 6-month period were reviewed retrospectively.

During the period under study, central venous catheters were inserted when one or more of the following indications were fulfilled:

1. To monitor central venous pressure when this was considered a desirable aid in management.
2. To withdraw venous blood samples when frequent laboratory estimations were necessary.
3. To infuse intravenous fluids and drugs over a prolonged period when peripheral veins were scarce or difficult to cannulate.
4. To infuse hypertonic intravenous feeding solutions.

The central venous catheters were inserted by rotating residents and medical students under supervision of the residents. The insertion site of first choice was the basilic vein in either antecubital fossa, but when these sites were not available the cephalic vein in the deltopectoral groove or the external jugular vein was occasionally used. A standard 95-cm polyethylene catheter, of external diameter 2·08 mm, with a radio-opaque marker line (Argyle Medicut sentinel line catheter), was inserted by surgical cutdown. Catheters were not sharpened and were inserted until free aspiration of blood and easy flow of the intravenous solution suggested that the tip was located in a central vein. The catheter was then

---

* Intensive Care Unit, University of Alberta Hospital, Edmonton, Alberta, Canada.

Requests for reprints to Mr T. E. B. Dane, Department of Surgery, Adelaide Hospital, Peter Street, Dublin 8, Ireland.

policy and practice is to assume that deep irradiation can confer extra therapeutic benefits and that certain patients should have the additional help that irradiation offers.

In young patients (under 35 years of age) the operation is not performed without some preoperative radiotherapy. Similarly, in all patients under the age of 45 and in many under the age of 55 preoperative radiotherapy is advised because of the fear that the handling at operation of a lung growth in patients of this age may favour dissemination.

In closing a discussion on preoperative irradiation Shields (Shields et al., 1970) said that he felt like an unappreciated St George, for he had hoped to kill the dragon of the routine use of deep X-ray therapy. He claimed that his results showed that though you can operate upon more patients following preoperative irradiation, you do not save any more than without it.

The present author's experience with radiotherapy *after* operation has been generally disappointing. If an inoperable growth is disclosed there may be a good case for radiotherapy but its value is uncertain, and in the author's experience no case found to be inoperable at thoracotomy became operable after postoperative irradiation.

The development of a new lung cancer

It is desirable to consider the development of a new lung cancer in patients who have been cured of one cancer of the lung. Clearly this very interesting biological occurrence could not be observed until successful operation had provided prolonged survival. It is remarkable that lung cancer caused or activated by an external irritant does not frequently occur in more than one site. Nature can be prodigal in her gifts and bilateral lung cancer now has a considerable literature devoted to it.

Hughes and Blades (1961) recorded 2 cases of a second lung cancer occurring 9 and 10 years respectively after resection of the original primary. Le Gal and Bauer (1961) surveyed the literature and recorded 4 cases of a second lung cancer in 63 patients who had survived for 30 months or more after resection of their first growth. Watson (1965), in a study of 10-year survival in lung cancer, considered a group of 2540 cases suitable for a 10-year study and found 56 survivors. A second lung cancer developed in 4 of these 10-year survivors.

In the present series of 293 patients 2 had a bilateral growth for which simultaneous resection was done but without success. Nine other patients developed a *new primary growth* or what appeared to be one.

In 1 patient who had a right lower lobectomy in 1945 for a squamous-celled carcinoma, a new primary squamous-celled growth appeared in the left upper lobe in 1961, that is 16 years later, and this was successfully removed with conservation of the lingula, and he remains well 13 years later. In addition to these 9 cases a tenth patient who had a pneumonectomy done by an assistant in 1953 developed a new primary in his right lower lobe 10 years later. This patient had continued to smoke 20 cigarettes a day since his first operation, and the patient mentioned above whose new cancer was successfully resected had also continued to smoke after his first operation. A smoking history was not obtained in all the other patients, but at least 5 had not abandoned smoking. It is clear that a man or woman who has had a cancer of the lung successfully treated must be told that he must NOT smoke again.

References

BROCK SIR RUSSELL and WHYTEHEAD L. (1955) Radical pneumonectomy for bronchial carcinoma. *Br. J. Surg.* **43**, 8–24.

GRAHAM E. A. and SINGER J. J. (1933) Successful removal of an entire lung for carcinoma of the bronchus. *JAMA* **101**, 1371–1374.

HUGHES R. K. and BLADES B. (1961) Multiple primary bronchogenic carcinoma. *J. Thorac. Cardiovasc. Surg.* **41**, 421–429.

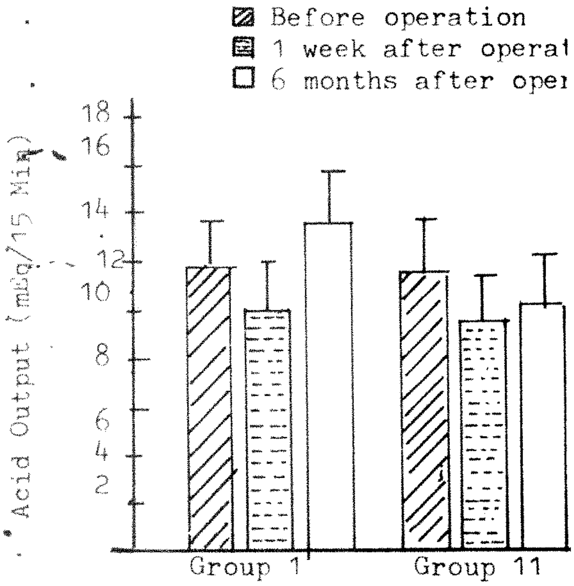
LE GAL Y. and BAUER W. C. (1961) Second primary bronchogenic carcinoma. A complication of successful lung cancer surgery. *J. Thorac. Cardiovasc. Surg.* **42**, 114–124.

MEDICAL RESEARCH COUNCIL (1966) Comparative trial of surgery and radiotherapy for the primary treatment of small-celled or oat-celled carcinoma of the bronchus. *Lancet* **2**, 979–986.

RUCKDESCHEL J. C., CODISH S. D., STRANAHAN A. and MCKNEALLY M. F. (1972) Postoperative empyema improves survival of lung cancer. *New Engl. J. Med.* **287**, 1013–1017.

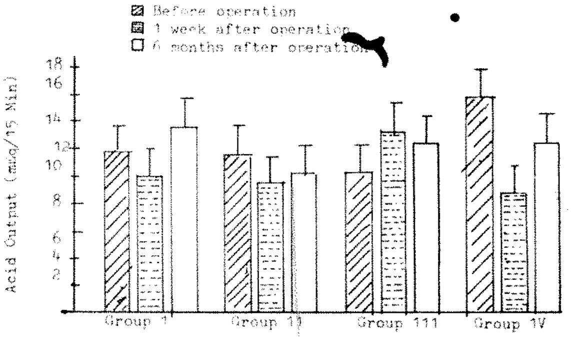
SHIELDS T. W., HIGGINS G. A., LAWTON R., HEILBRUNN A. and KEEHN R. I. (1970) Pre-operative X-ray therapy as an adjuvant in the treatment of bronchogenic carcinoma. *J. Thorac. Cardiovasc. Surg.* **59**, 49–61.

WATSON W. L. (1965) Ten-year survival in lung cancer. A study of 56 cases. *Cancer* **18**, 133–135.

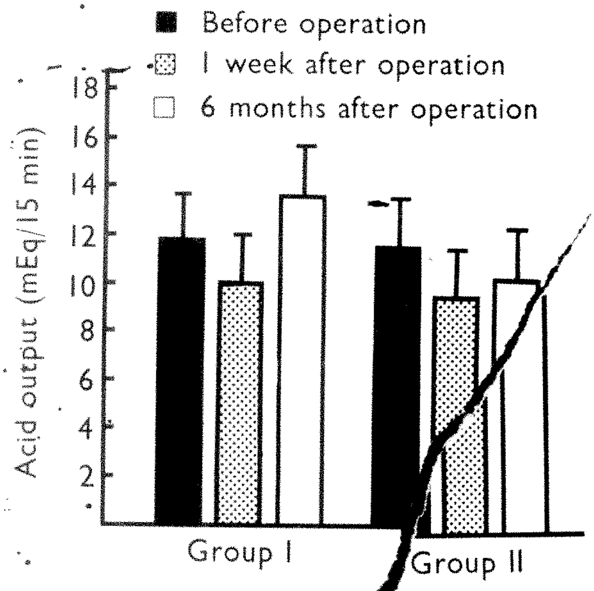


◀ SECTION OF ORIGINAL RECEIVED FROM AUTHOR

▼ ORIGINAL REDUCED TO REQUIRED SIZE

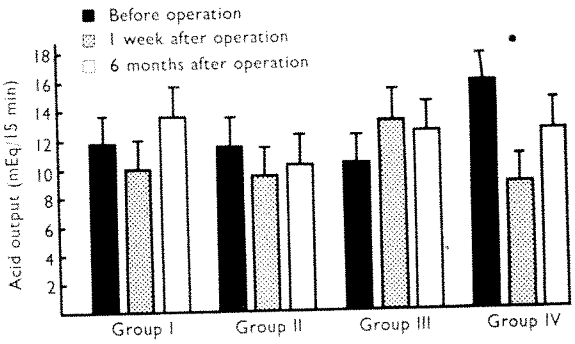


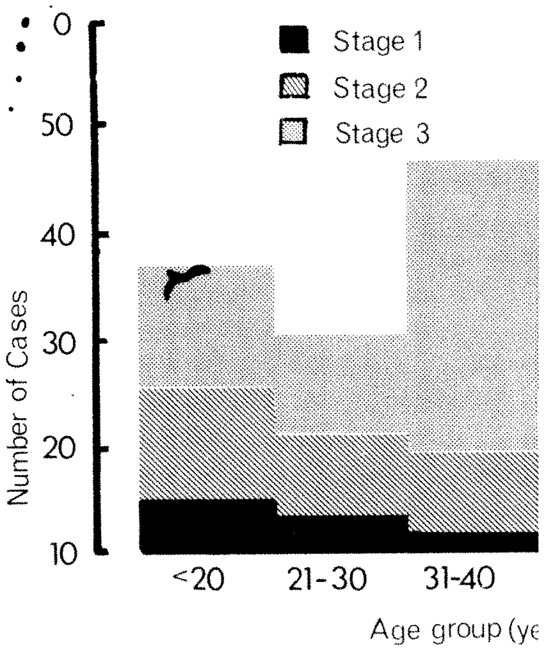
The above type of illustration conveys information, but the author probably did not expect it to be reproduced without redrawing. The typewritten annotations are not acceptable. The figures are not properly placed with respect to the scale, the use of the Arabic numeral 1 for Roman numerals along the bottom axis is incorrect, and of course the entire drawing is too rough to be acceptable in a journal. In the redrawn version all of these points have been taken care of, and the three columns have been more clearly differentiated by the use of black, white and a stipple of sufficient size to reproduce satisfactorily at the reduced scale.



◀ SECTION OF REDRAWN VERSION

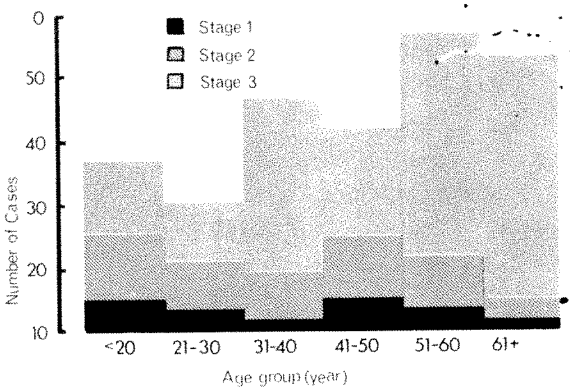
▼ REDRAWN VERSION REDUCED TO REQUIRED SIZE





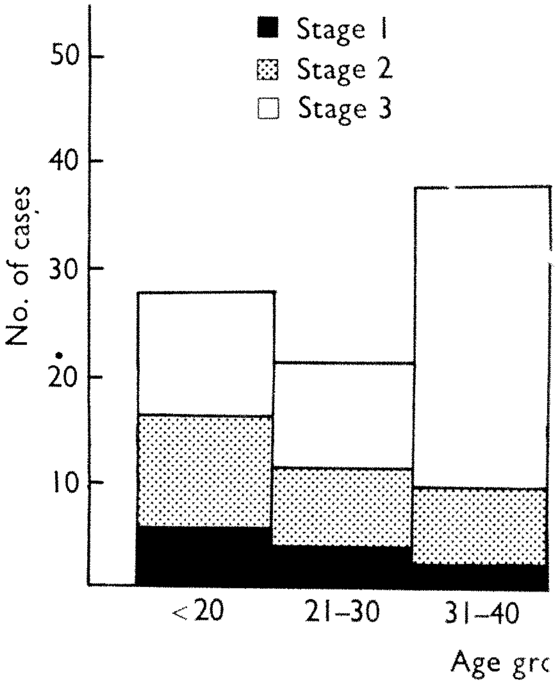
◀ SECTION OF ORIGINAL RECEIVED FROM AUTHOR

▼ ORIGINAL REDUCED TO REQUIRED SIZE



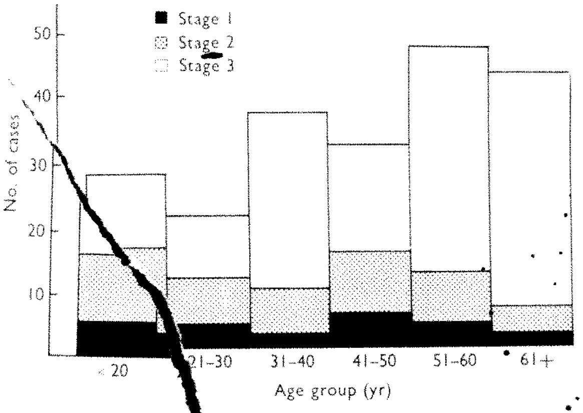
At first sight the artwork, of which a portion is reproduced at the same scale above, appears to have been quite carefully produced. Clear lettering has been applied, probably by Letraset, and two different tints have been used, probably from the same source. However, a reduction to the size necessary for printing in the Journal reveals the fact that the stipple used for stage three was too fine to give a smooth reproduction at a smaller scale. The problem which arises when two tints of this kind meet is also shown.

In most places an even white margin has been achieved, but where even the slightest overlap has been allowed to occur an unpleasant interference pattern develops, as between the 51–60 column and the 61+ column. The heading Age group (year) shows the difficulty of maintaining accurate alignment of the type of lettering used. In the redrawn versions, shown below, the section of the full scale reproduction shows how much larger the stipple needs to be in order to reproduce satisfactorily at a reduced scale. The lettering has been typeset in accordance with the typographical style of the Journal, and pasted on to the artwork. It will also be seen how much clearer this type of diagram is when the columns are outlined.



◀ SECTION OF REDRAWN VERSION

▼ REDRAWN VERSION REDUCED TO REQUIRED SIZE



Artwork for The British Journal of Surgery

NOTES FOR THE GUIDANCE OF ILLUSTRATORS

The Editorial Board of the *British Journal of Surgery* are very anxious to improve the standard of the illustrations used in articles published in the Journal. In general, they feel that little criticism can be directed at the photographs supplied by authors, but that frequently line illustrations, charts and graphs have in the past appeared in an unsatisfactory form. The attention of authors is therefore drawn to the brief notes on this subject given under the heading 'Instructions to Authors' under Editorial Notices among the preliminary pages of each issue of the Journal.

The following additional notes have been prepared for the guidance of authors and their artists, but it is intended in future to subject artwork submitted to a somewhat more critical examination than heretofore, and in cases where the artwork is found to be unsuitable for reproduction, to refer it back to authors for improvement. At the same time, the publishers are able to offer a service for the re-lettering, the improvement or the total redrawing of artwork at a moderate cost if this should prove more convenient to authors than recommissioning the work themselves. The cost of redrawing a simple block diagram with some lettering could be of the order of £4, while a highly detailed anatomical drawing could involve a charge of £15 at mid-1974 costs.

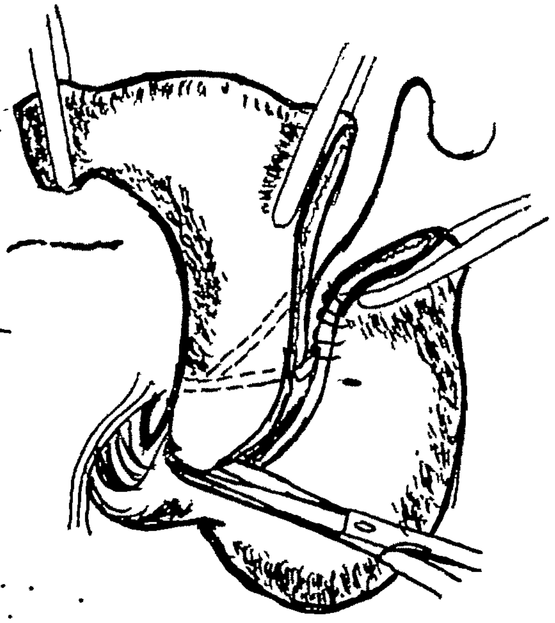
It should be borne in mind that an artist will normally draw a diagram at a considerably larger scale than would be appropriate for reproduction in the pages of a journal, where space is at a premium. The artist must consequently bear in mind that when his drawing is photographically reduced in size the thickness of every line and the size of all lettering will be proportionately reduced; unless due allowance for this subsequent process is made at the drawing stage the end result may well have lines and symbols that are so light in weight as to be scarcely visible and lettering so small and crowded as not to be easily legible.

Since the Journal has been re-styled it will be noted that whenever possible line diagrams are reproduced at column width, i.e. 74 mm. Sometimes it may be necessary to use the full page width of 152 mm and, rarely, an intermediate width can be accommodated. The ideal line width for the main axes of graphs or charts as printed is approximately $\frac{1}{2}$ mm, about $\frac{1}{8}$ mm or $\frac{1}{4}$ mm being regarded as the lightest line weight that should normally be used for detail.

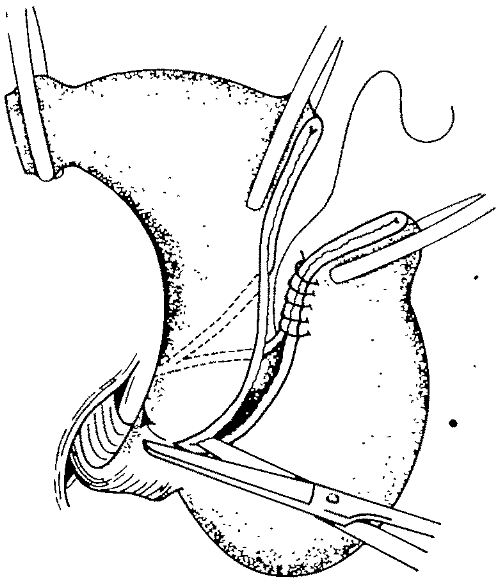
Another problem frequently arises with shading, or with various types of cross-hatching used, for example, in histograms. In these cases it is quite common for the artist to space the shading lines in such a way as to look most satisfactory on the original artwork, but on reduction in size the lines are seen to merge together and so produce an unsightly and irregular effect. Relatively open shading should always be used.

Lettering—as already mentioned in the Instructions for Authors—should be in sans serif style, and it should be drawn at such a size as to reproduce no smaller than 3 mm. from the top of the capital letter to the bottom of a descending letter, such as y. General titles, descriptive headings and units along the axes of graphs should be slightly larger.

▼ ORIGINAL ILLUSTRATION RECEIVED FROM AUTHOR



▼ REDRAWN VERSION OF ILLUSTRATION



This reproduction of the type of drawing sometimes received contrasts with the professionally redrawn version alongside. From many points of view the rough detail in the original version would have looked better at a reduced scale, but in fact the effect of reduction would have been to clog up much of the detail, and produce an even rougher appearance.

5 years or more; that is 24 per cent of those who had an operation and 30 per cent of those who survived operation.

Radical pneumonectomy

Table V shows the figures for this operation. *Table VI* shows the long term survival after operation. Thirty-nine patients lived 5 years or more; that is 33 per cent of those who had an operation and 39 per cent of those who survived operation.

Comparative results

These are presented in *Table VII*. One patient had bilateral lobectomy with an interval of 16 years and 2 patients had simultaneous bilateral lobectomy and segmental resection and lobectomy respectively.

The 5-year survival is based on the number of patients surviving operation and not on those originally submitted to operation.

It is common to find the 5-year survival rate after lobectomy to be high, e.g. 40–50 per cent, but this is in essentially a selected group. In the present series it was 41 per cent. A search of the world literature failed to find a 5-year survival rate after pneumonectomy of over 33 per cent. The 5-year survival rate after radical pneumonectomy of 39 per cent in the present series is significant. This is almost the same as the survival rate after lobectomy (41 per cent) and it suggests that radical pneumonectomy does improve the chance of 5-year survival.

Irrespective of the type of operation, it is noteworthy that in patients in whom removal of the growth is possible there is a 1 in 3 chance of 5-year survival. This can be comforting and encouraging knowledge to give to a patient or his relatives.

The object of the radical operation is to try to catch in the wider surgical net lymph nodes that are involved by the growth and which would otherwise not be removed. Some indication of what is achieved is given in *Table VIII*. The diminished survival rate when nodes are invaded is clearly shown and corresponds with all published experiences. On the other hand, 9 patients in whom invaded nodes were removed lived for more than 5 years after operation. Without a radical operation they could scarcely have survived for so long. Some of these patients have survived for much longer than 5 years after removal of invaded lymph nodes, as is shown in *Table IX*. Six survived for more than 10 years and 3 are still alive 13, 16 and 24 years respectively after operation.

Nine patients in whom the nodes were not involved at operation are still alive after 25, 23, 22, 20, 15, 15, 15, 9 and 8 years respectively.

After this separate presentation of the results of three different types of resection it is desirable to present the combined figures of long term survival. These are shown in *Table X*.

Table VIII: SIGNIFICANCE OF NODAL REMOVAL BY RADICAL PNEUMONECTOMY

	Nodes	
Patients	Invaded	Not invaded
Total	48	52
Dead	45	43
Still alive	3	9
Lived > 5 yr	9	30

Table IX: LENGTH OF SURVIVAL WITH NODAL INVOLVEMENT

Survival (yr)	No. of cases	Still alive
5–6	2	—
6–7	1	—
12–13	2	1
16	3	1
24	1	1
Total	9	3

Table X: LONG TERM SURVIVAL IN 293 CASES

Survival (yr)	No. of cases	Still alive
5+	21	1
6–10	31	6
11–15	20	5
16–20	10	3
21–25	7	4
26–30	5	4
34	1	1

Comments on long term survival

As malignant disease commonly occurs in middle-aged or elderly people it is clear that in a long follow-up deaths may occur from causes unconnected with the malignant disease itself. Thus age alone may be the cause. The earliest long-surviving patient in this series was aged 49 when he was operated on in 1939. His death nearly 26 years later at the age of 75 was, therefore, not unusual. Similarly, a man aged 63 who had a lobectomy in 1941 came to a natural end 21 years later at the age of 84. These are only two examples of many similar cases. In 1940 a man aged 43 underwent pneumonectomy and is now, 34 years later, 76 years old and the longest survivor in this series. His natural expectation of life must inevitably be short.

In a large series such as this with patients coming from many countries of the world some are inevitably lost to follow-up. This has been so in 11 cases and death has been assumed at the date of the last information. On the other hand, persistent search has often brought unexpected news of a good result. Thus a woman operated on at the age of 31 in 1943 was lost to follow-up in 1963 but was found to be still alive and well in 1973, 30 years after the operation.

Two unusual cases merit special mention. A man aged 52 underwent right lower lobectomy for a squamous-celled carcinoma in 1945; in 1961 at the age of 67 he developed a new carcinoma of the left upper lobe for which a lobectomy was done. He is still alive and well 13 years later at the age of 81! In 1949 a woman aged 27 presented with a hopelessly inoperable carcinoma of the right main bronchus with extensive carinal node involvement. She was treated with deep irradiation and some 6 months later was able to undergo a radical pneumonectomy. She is still alive 24 years later.

These 2 cases, and certain others, impress one with the importance of a biological factor being present

Table XI: HISTOLOGICAL TYPE OF THE TUMOUR IN 272 CASES

Type	No. of cases
Oat-celled	46
Anaplastic or undifferentiated	35
Squamous-celled	139
Adenocarcinoma	36
Columnar-celled	11
Transitional-celled	5

that determines cure or early recurrence and death. As a surgeon one excusably takes some credit for long freedom from recurrence and even apparent cure (as for example when 34 years have passed since operation), but in spite of this we should be wrong to attribute all our success to our surgery when it is more probable that some favourable biological factor has been present and responsible. Conversely, in cases in which operation has been done early and apparently efficiently and yet recurrence kills the patient in a few months, an adverse or unfavourable biological determining factor may well be present. It would be wrong in the one case to assign very great credit to surgery, just as in the other case it would be wrong to attribute all the failure to surgery. Some other deeper process is involved, although as yet imperfectly understood. Advance in the treatment of cancer of all types must wait until we understand more fully the biological factors involved and how we can control them. Operation alone can never achieve this and, indeed, few surgeons would disagree that the time will come when cancer can be controlled by some process, doubtless biological, that enables us to dispense with the unpleasant, often mutilating and uncertain operations that we now must do, just as the advent of antibiotics has seen the revolution in the management of infective processes.

One well-recognized and frequently documented factor involved in the varying prognosis in lung cancer is the histological type of the tumour; that is, the cellular composition. This seems to involve a biological factor of great importance. A few simple conclusions emerge from a consideration of the histological nature of the growths in this series.

Three examples of sarcoma occurred. No histology is available in 18 cases. Of the remaining 272 cases, the histology is shown in *Table XI.*

The allocation to one specific type often varies with the individual histologist. The groups of 'anaplastic' or 'undifferentiated' carcinoma are especially uncertain and only a general assignment is possible.

In great contrast to the squamous-celled are the oat-celled and anaplastic or small-celled growths. Of patients with the former, 42 survived operation for an average of 3 years; of those with the latter, 30 survived operation for an average of just over 3 years.

The author has never been impressed with the conclusions published in the Medical Research Council's report in 1966. This had the objections of far too numerous participants (50 surgeons) over too short a time (2 years). Their essential recommendations were that operation offered very little in the oat-celled and small-celled types of growth and that slightly better results could be achieved by radiotherapy. Many thoracic surgeons have had similar experiences to the author with this type of growth, namely that although in general the prognosis is poor, long survival can sometimes be achieved.

One of the early patients in this series, operated on in 1939, had an oat-celled carcinoma and he lived for over 25 years until the age of 75. Of the 73 patients with an oat-celled or small-celled carcinoma who survived operation, 8 lived for between 5 and 10 years, 7 more than 10 years and 2 over 20 years (24 and 25 years respectively). From this experience it would be wrong to reject operation in the treatment of all oat-celled or small-celled growths.

Favourable biological factors have been mentioned in general terms, but there are other factors that appear to be more favourable.

Empyema and long survival

The patient with an oat-celled cancer who lived for more than 25 years developed an empyema after his pneumonectomy, and it has been suggested by several authors and most recently by Ruckdeschel et al. (1972) that the development of a pleural infection may be favourable to long survival by enhancing the body's natural resistance to the cancer; just as was suggested in the case of sarcoma by Coley. Two other patients in the present series who were operated on in 1940 also developed an empyema. One lived for 27 years and then died of a new cancer in the remaining lung; the other patient is still alive 34 years later. It is noteworthy that Graham's first successful pneumonectomy patient developed a pleural infection and survived 30 years (Graham and Singer, 1933).

The occurrence of an empyema after pneumonectomy can be a serious event and may result in early death rather than prolonged survival.

In the whole series of 293 cases a postoperative empyema occurred in 27 patients (3 who had a lobectomy and 24 who had a pneumonectomy).

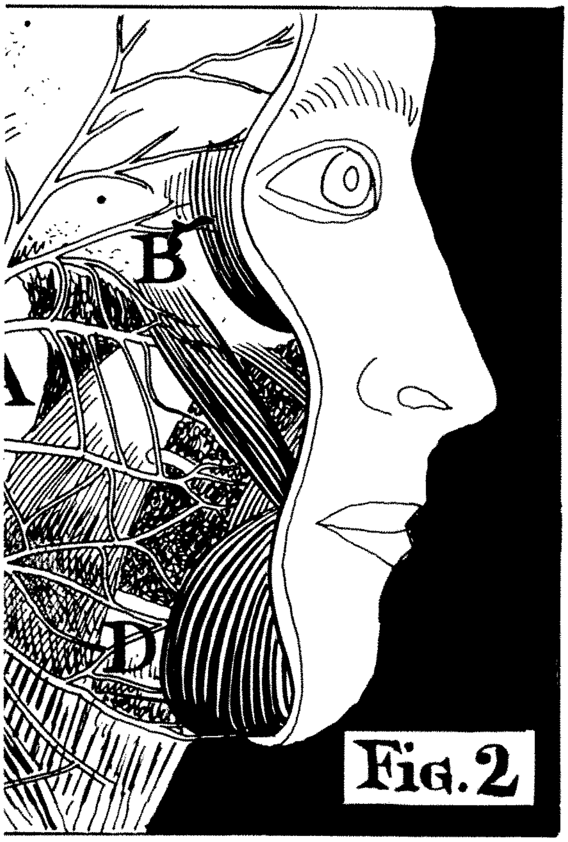
Of the 24 patients who had an empyema after pneumonectomy, 12 lived for more than 5 years, that is 44·4 per cent. This is definitely higher than the 5-year survival rate for simple pneumonectomy which is 30 per cent in this series. Eleven patients lived for more than 10 years (40·74 per cent) and 4 for over 20 years (20 per cent).

From these figures it would appear that the occurrence of a pleural infection may be favourable to long survival probably because of some immunological factor.

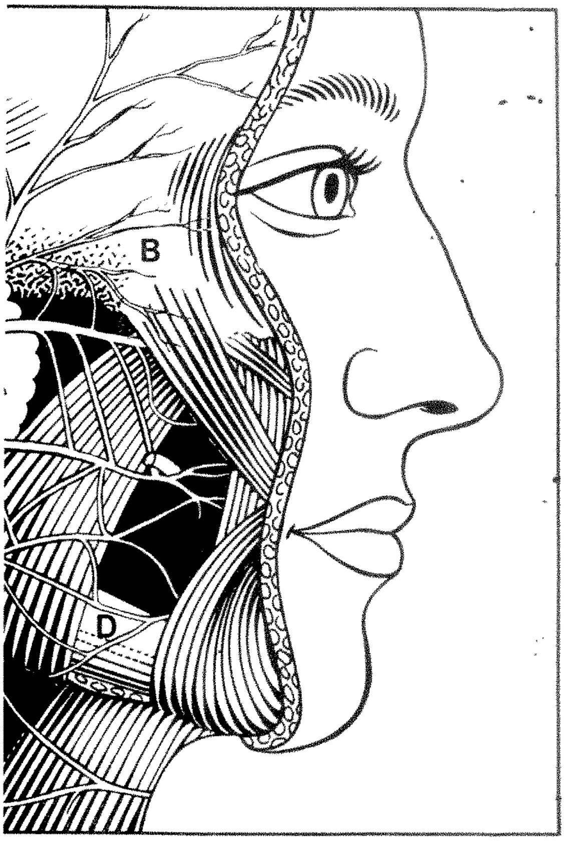
Radiotherapy

The best treatment for a lung cancer is to excise it. Radiotherapy alone can rarely cure a patient and is disappointing in the prolongation of life that it confers. There is good evidence from many authors that it can convert an inoperable cancer into one that can be removed, as in the case cited earlier. A question that we must ask is whether preoperative irradiation can increase the chance of cure or of long survival when the growth appears to be operable. The author's

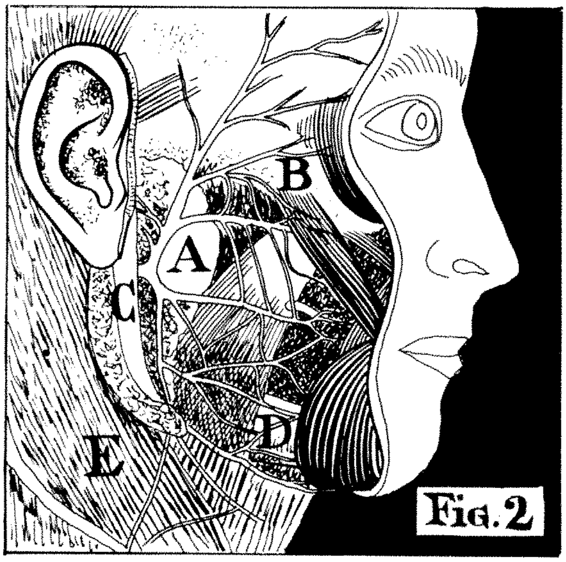
▼ SECTION OF ORIGINAL RECEIVED FROM AUTHOR



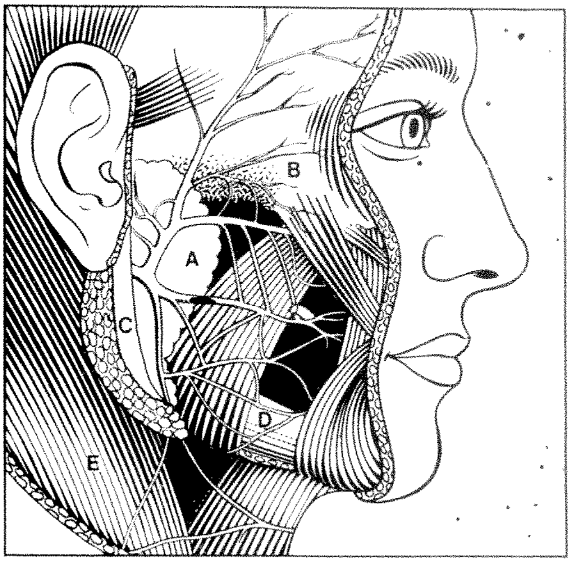
▼ SECTION OF REDRAWN VERSION



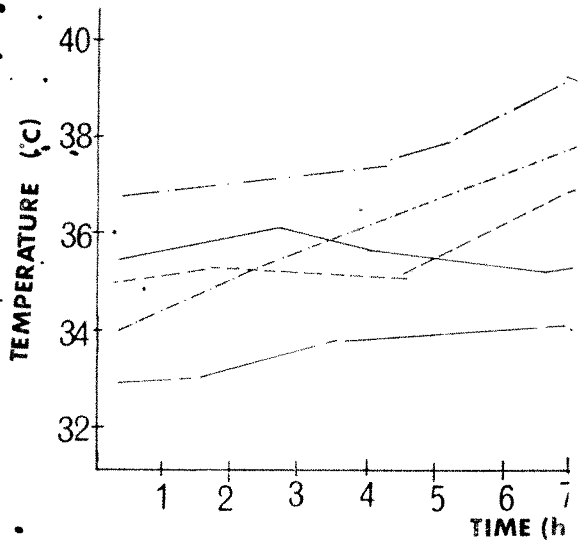
▼ ORIGINAL REDUCED TO REQUIRED SIZE



▼ REDRAWN VERSION REDUCED TO REQUIRED SIZE

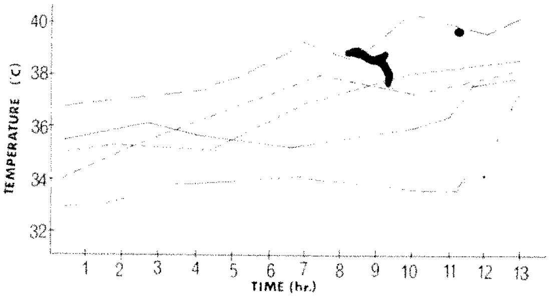


The original drawing, of which part is reproduced as drawn, has been carefully, if amateurishly, executed. It particularly illustrates the danger of the filling-in of detail when such a drawing is reduced in scale. The lettering has been inexpertly added, and for the *British Journal of Surgery* we prefer not to have the figure number on the drawing itself as it always occurs in the legend. The comparison of these two versions would repay careful study on the part of an artist.

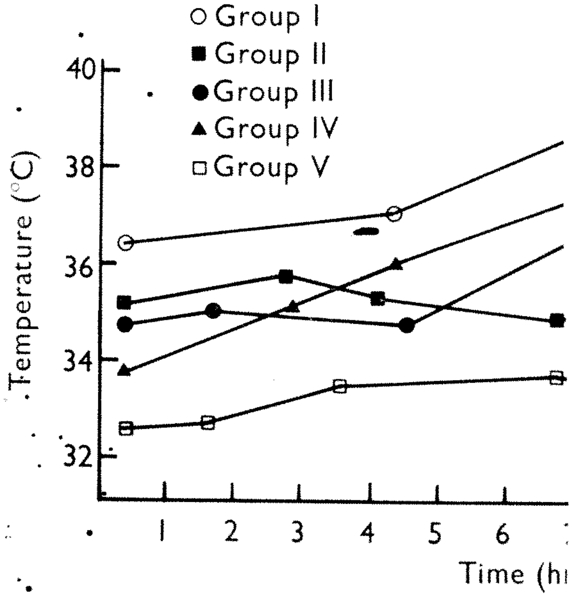


◀ SECTION OF ORIGINAL RECEIVED FROM AUTHOR

▼ ORIGINAL REDUCED TO REQUIRED SIZE

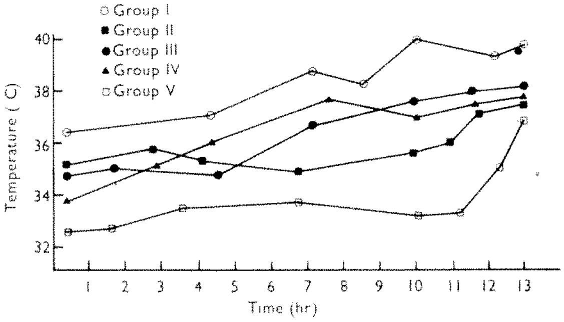


The section of the piece of original artwork shown above particularly illustrates the danger of using too light a weight of line, for it will be seen that when reduced to the appropriate size some of the lines have become so thin as not to reproduce evenly. The difficulty of maintaining accurate positioning of Letraset lettering is also shown in the numbers along the baseline The redrawn version of the artwork shown below indicates how much heavier the original needs to be to give really satisfactory reproduction at the reduced scale. A preferred method of differentiating between graph lines is also shown. A key to the five different curves has been added and the importance of this cannot be over-estimated.



◀ SECTION OF REDRAWN VERSION

▼ REDRAWN VERSION REDUCED TO REQUIRED SIZE



ligated in the vein and fixed to the skin by a suture. When no peripheral veins were available, catheters were inserted percutaneously into a major vein, and the subclavicular approach to the subclavian vein was the route most commonly used. A 30-cm, 21-gauge catheter in an 18-gauge needle (Venocath, Abbott Laboratories) was used for these insertions.

The location of the catheters was checked immediately after insertion by obtaining a portable chest X-ray while injecting 5 ml of sodium diatrizoate 50 per cent (Hypaque) through the catheter. Those shown unkinked and with their tip in the subclavian or innominate vein, the superior vena cava or the right atrium were accepted as suitably placed. Catheters that had failed to enter the central venous system or those that passed retrogradely into the interior jugular vein were replaced or manipulated and the X-ray repeated. Catheters that were coiled in the central venous system or too far advanced into the inferior vena cava or the heart were repositioned by withdrawing them an estimated distance. Under these circumstances a repeat X-ray was often omitted.

The insertion sites were dressed daily using polymyxin B, neomycin and mycostatin ointment. Catheters were not changed regularly and were removed only when no longer required or when some catheter complication developed.

Results

Ninety (75 per cent) of the 120 patients admitted during the period studied had one or more attempts to insert a central venous catheter. Eighty-one (90 per cent) of these had a catheter inserted into the central venous system after one to three attempts. Twenty-four (80 per cent) of 30 further attempts succeeded in locating a second catheter in the central venous system. During all these attempts, catheters that failed to enter the central veins were either stuck in the axillary vein or entered the internal jugular vein retrogradely. Direct puncture of major veins was used to insert 33·3 per cent of second catheters, but only 4·4 per cent of first catheters. *Table I* shows the success rate for each attempt for both first and second catheters.

All the catheters that did enter the central venous system were not located in suitable positions within it. The actual locations of these and the various sites from which they were inserted are shown in *Table II*.

Table I: CATHETERS LOCATED IN CENTRAL VENOUS SYSTEM AFTER VARIOUS INSERTION ATTEMPTS

Central venous catheter	Insertion attempt	No. of attempts	Catheters located in central veins No.	%
First	First	90	61	67·8
First	Second	29	14	48·3
First	Third	15	6	40
First	All attempts	134	81	60·5
Second	First	30	24	80
First and second	All attempts	164	105	64

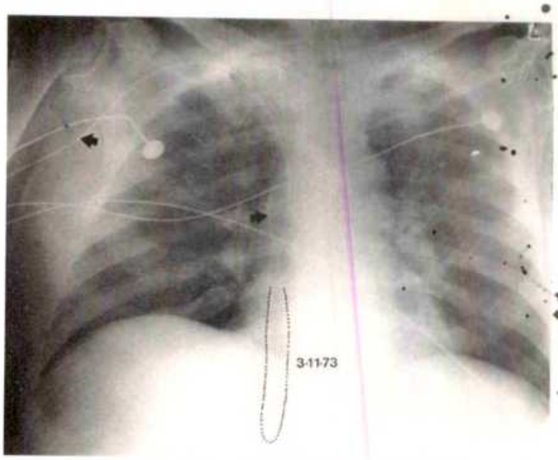


Fig. 1. Chest X-ray taken after the insertion of a catheter in the right arm on day 36. Note the catheter coiled in the right atrium and superior vena cava.

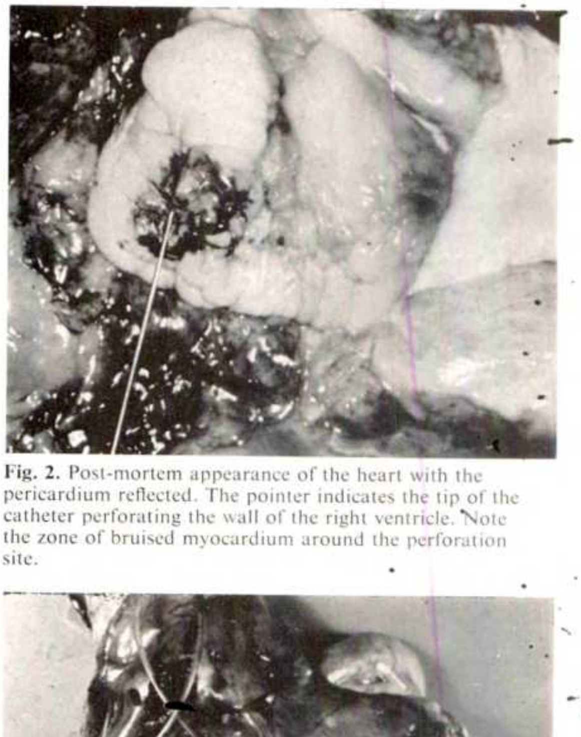


Fig. 2. Post-mortem appearance of the heart with the pericardium reflected. The pointer indicates the tip of the catheter perforating the wall of the right ventricle. Note the zone of bruised myocardium around the perforation site.

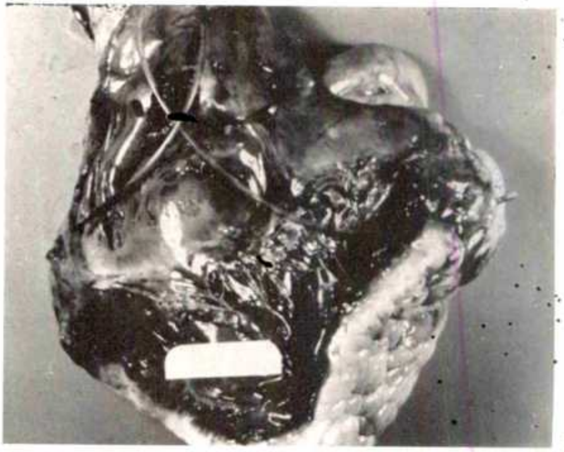


Fig. 3. Heart opened at post-mortem to show the two catheters in the right atrium. The catheter from the right arm crosses the tricuspid valve and perforates the anterior wall of the right ventricle.

Table II: LOCATION OF CATHETERS IN CENTRAL VENOUS SYSTEM AFTER INSERTION FROM VARIOUS SITES

		Location of catheters in central veins			
Insertion site	Catheter in central veins	Innominate veins or SVC	Right atrium	Other intracardiac sites	Coiled in central veins
Right basilic vein ($n = 95$)	64	23	18	9	14
Left basilic vein ($n = 35$)	23	14	4	3	2
Cephalic vein ($n = 20$)	4	4	0	0	0
All arm veins ($n = 150$)	91 (60·7%)*	41 (45·1%)†	22	12	16
Major veins ($n = 14$)	14 (100%)*	9 (64·3%)†	3	0	2
All sites ($n = 164$)	105 (64%)*	50 (47·6%)†	25	12	18

SVC, Superior vena cava.
* Percentage of all attempts from given insertion site.
† Percentage of all catheters located in central venous system from given site.

Table III: MECHANICAL COMPLICATIONS (TOTAL OF 105 CATHETERS)

Complication	No. of catheters	% of total catheters
Cracked catheters	13	12·4
Thrombophlebitis	4	3·8
Cardiac arrhythmias	2	1·9
'Lost' catheters	1	0·95
Cardiac tamponade	1	0·95

The locations given were those seen on the final X-ray taken and, although the malpositioned catheters were relocated by partial withdrawal, repeat X-rays were not done.

The catheters remained *in situ* from 1 to 65 days with an average duration of 12 days. While they were *in situ*, 21 (20 per cent) of the 105 catheters produced some mechanical complication (*Table III*).

Cracks in the catheters all occurred in the exposed portion and in most cases well away from the insertion site. These cracks were usually revealed by leakage of intravenous fluid. The cases with thrombophlebitis were all diagnosed clinically and catheters were sterile on culture when removed. Cardiac arrhythmias consisted of multiple premature ventricular contractions, which in one patient compromised cardiac output for a brief period. In both cases the catheter was located in the pulmonary outflow tract and the arrhythmia disappeared immediately when the catheter was withdrawn. The one 'lost' catheter broke and disappeared into the left basilic vein. A plain X-ray of the upper arm showed its retracted end situated 5 cm above the medial epicondyle. It was retrieved by local cutdown and the patient suffered no ill effects. The case of cardiac tamponade is the one described in the present case report.

Discussion

Cardiac tamponade due to perforation of the heart wall by a polyethylene catheter was first described by Brown and Kent (1956). Their patient died from cardiac tamponade due to perforation of the wall of the right ventricle by a fragment of a polyethylene catheter lost into the femoral vein 80 days earlier. Friedman and Jurgeleit (1968) then reported a fatal cardiac tamponade secondary to perforation of the wall of the right atrium by an intact polyethylene central venous catheter. Fourteen further cases of cardiac tamponade caused by perforation of the heart wall by intact polyethylene catheters have been reported (Barton et al., 1968; Kline and Hofman, 1968; Thomas et al., 1969; Brandt et al., 1970; Fitts et al., 1970; Adar and Mozes, 1971; Homesley and Zelenik, 1971; Bone et al., 1973). Defalque (1971) reported cardiac tamponade almost immediately after subclavian puncture, and at post-mortem the tip of the catheter was piercing the superior vena caval wall just below the site of pericardial reflection. McHenry and Hopkins (1968) reported cardiac tamponade caused by fluid infused through an open-ended pacing electrode which had perforated the wall of the right ventricle 60 hours after insertion. All but one (Defalque, 1971) of these accidents conform to a very similar pattern which is also true of the case reported in this paper. The polyethylene catheters were introduced through arm veins, their locations after insertion were either not checked radiologically or they were located in the right atrium, the patients were asymptomatic for periods of 30 minutes to 9 days and then each suffered a rapid drop in arterial blood pressure. The fluid found in the pericardial sac was the same as that being infused via the catheter, and varied from 200 to 1000 ml in volume. Three patients (Barton et al., 1968; Thomas et al., 1969; Brandt et al., 1970) were resuscitated after aspiration of the pericardial space but they subsequently died, having suffered irreversible brain damage. Two cases caused by polyethylene catheters (Thomas et al., 1969; Brandt et al., 1970) and 1 case caused by fluid infused through a pacing electrode (McHenry and Hopkins, 1968) made full recoveries after aspiration of the fluid.

Although this form of cardiac tamponade is rare, the mortality rate it carries is distressingly high. The problem should be preventable by locating all central venous catheters outside the heart.

The review of catheter locations presented in this paper shows a high incidence of catheter malposition which includes failure to enter the central venous system and malposition within the central veins. Fifty-nine (39·9 per cent) of 150 catheters inserted via peripheral arm veins lodged in the axillary, the cephalic or the internal jugular veins. After manipulation or replacement only 9 (10 per cent) of the 90 patients did not have a catheter in the central venous system. Although we found that this form of catheter malposition was not a problem with insertion by major vein puncture, we have refrained from using it as our first choice of insertion site, as it has been associated with dangerous complications (Smith et al., 1965; Schapira and Stern, 1967; Wiseheart et al., 1972). Failure to enter the central venous system will not cause cardiac tamponade but unless it is detected unreliable or misleading central venous pressure measurements will be recorded (Gilday and Downs, 1969; Dietel and McIntyre, 1971; Langston, 1971; Thomas, 1972).

Catheter malposition within the central venous system can, however, cause dangerous mechanical complications as well as unreliable central venous pressure readings. This review of 105 catheters showed that 25 (23·8 per cent) were located in the right atrium, 12 (11·4 per cent) were in other intracardiac sites and 18 (17·1 per cent) were coiled in the superior or inferior vena cavae. Some of this malpositioning may have been due to the use of a 95-cm catheter. Fourteen (60·9 per cent) of the 23 catheters inserted from the left arm but only 23 (35·9 per cent) of the 64 inserted from the right arm were located in the superior vena cava. These long catheters were probably inserted too far but the extra length was accommodated better in the longer venous route from the left arm. A 52·5-cm catheter is now used and not more than 45 cm are inserted until a check X-ray is done. There is considerable confusion in the literature about where central venous catheters should be located. An early description of the use of central venous pressure measurements specified that the catheter tip should lie at the junction of the innominate veins and the superior vena cava, and that the inferior vena cava should be avoided (Wilson et al., 1962). However, some recent writers (Bethel, 1972; Colvin et al., 1972) have suggested that the right atrium should be used routinely, and others (Bell et al., 1973) use the superior vena cava and the right atrium as suitable positions. Guyton and Jones (1973) has shown that the venous pressure at any site within the great veins or venae cavae is within 1 mm Hg of that in the right atrium. The subclavian vein usually has a pair of valves situated within 2 cm of its termination (Warwick and Williams, 1973), and Thomas (1972) suggested that catheters should be advanced into the subclavian vein beyond the narrow, easily compressed costoclavicular segment where arm movement may induce vein wall trauma by the tip of the catheter. Bansmer et al. (1958) showed that catheters in the inferior vena cava were associated with a very high thrombosis rate, and Wilson et al. (1962) suggested that venous pressures within the inferior vena cava are unreliable in the presence of abdominal distension. From these facts and our experience of cardiac perforation by an intracardiac catheter we suggest that all central venous catheters should be located in the innominate (brachiocephalic) veins or the upper half of the superior vena cava.

Although the original 95-cm catheter had a radio-opaque marker line, it was not possible to identify the catheter in the mediastinal shadow of the portable chest X-rays used in the intensive care unit. The catheter now used (Sorenson Intrafusor, 52·5 cm) has a better defined marker line that can be identified easily on plain chest X-rays. This provides a useful check on catheter position during the time that it is *in situ* without repeating radio-opaque dye injection.

Cracked catheters were the most frequent mechanical complication noted in this review. These are not dangerous if detected early and replaced, but Wellman et al. (1968) found that they were a frequent forerunner of 'lost' catheters. The one lost catheter in this review occurred after a cracked catheter had been repaired by removing the damaged portion and reconnecting the intravenous fluids line through a blunt needle. This practice is dangerous and has been discontinued. All cracked catheters should be removed and replaced if there is still need for a central venous line.

Conclusions

The following guidelines for the insertion and use of central venous catheters have been formulated from the data provided by this review and the experience of a fatal cardiac tamponade:

1. Catheters should be inserted via the basilic vein in the antecubical fossa unless the operator is skilled in performing subclavian puncture.
2. A 52·5-cm catheter with an adequate radio-opaque marker line should be used, and not more than 45 cm of catheter inserted until the first check X-ray is taken.
3. The catheter's location should be checked radiologically after insertion and each manipulation.
4. The catheter should be located, without coiling, in the innominate veins or the upper half of the superior vena cava.
5. The insertion site should be kept covered and dressed daily using a topical antibiotic ointment.
6. Cracked catheters should be removed and not repaired.

Acknowledgements

We extend our grateful thanks to the resident medical and nursing staff of the Intensive Care Unit who cared for these patients, to the filing room staff of the Radiology Department for their help with location of the X-rays and to Ms Kathy Tropeau who typed the manuscript.

References

ADAR R. and MOZES M. (1971) Fatal complications of central venous catheters. *Br. Med. J.* 3, 746.

BANSMER G., KEITH D. and TEALUK H. (1958) Complications following use of indwelling catheters of inferior vena cava. *JAMA* 167, 1606–1611.

BARTON J. J., VENECKO R. and GROSS M. (1968) Perforation of right atrium and resultant cardiac tamponade: a complication of catheterization to measure central venous pressure. *Obstet. Gynecol.* 32, 556–560.

BELL J. A., BRADLEY R. D. and JENKINS B. S. (1973) Malpositioning of central venous catheters. *Lancet* **1**, 105–106.

BETHEL H. J. N. (1972) Long term intravenous infusions. *Lancet* **2**, 433.

BONE D. K., MADDREY W. C., EAGAN J. and CAMERON J. L. (1973) Cardiac tamponade. A fatal complication of central venous catheterization. *Arch. Surg.* **106**, 868–870.

BRANDT R. L., FOLEY W. J., FINK G. H. and REGAN W. J. (1970) Mechanism of perforation of the heart with production of hydropericardium by a venous catheter and its prevention. *Am. J. Surg.* **119**, 311–316.

BROWN C. A. and KENT A. (1956) Perforation of right ventricle by polyethylene catheter. *South. Med. J.* **49**, 466–467.

COLVIN M. P., BLOGG C. E., SAVEGE T. M., JARVIS J. D. and STRUNIN L. (1972) A safe long-term infusion technique? *Lancet* **2**, 317–320.

DEFALQUE R. J. (1971) Fatal complication of subclavian catheter. *Can. Anaesth. Soc. J.* **18**, 681–682.

DEITEL M. and MCINTYRE J. A. (1971) Radiographic confirmation of site of central venous pressure catheters. *Can. J. Surg.* **14**, 42–52.

FITTS C. T., BARNETT L. T., WEBB C. M., SEXTON J. and YARBROUGH D. R. (1970) Perforating wounds of the heart caused by central venous catheters. *J. Trauma* **10**, 764–769.

FRIEDMAN B. A. and JURGELEIT H. C. (1968) Perforation of atrium by polyethylene CV catheter. *JAMA* **203**, 1141–1142.

GILDAY D. L. and DOWNS A. R. (1969) The value of chest radiography in the localization of central venous pressure catheters. *Can. Med. Assoc. J.* **101**, 363–364.

GUYTON A. C. and JONES C. E. (1973) Central venous pressure: physiological significance and clinical implications. *Am. Heart J.* **86**, 431–437.

HOMESLEY H. D. and ZELENIK J. S. (1971) Hazards of central venous pressure monitoring: pericardial tamponade. *Am. J. Obstet. Gynecol.* **109**, 1216–1217.

KLINE I. K. and HOFMAN W. I. (1968) Cardiac tamponade from CVP catheter perforation. *JAMA* **206**, 1794–1795.

LANGSTON C. S. (1971) The aberrant central venous catheter and its complications. *Radiology* **100**, 55–59.

MCHENRY M. M. and HOPKINS D. M. (1968) Cardiac tamponade as a result of infusion. *JAMA* **203**, 167–168.

SCHAPIRA M. and STERN W. Z. (1967) Hazards of subclavian vein cannulation for central venous pressure monitoring. *JAMA* **201**, 111–113.

SMITH B. E., MODELL J. H., GAUB M. L. and MOYA F. (1965) Complications of subclavian vein catheterization. *Arch. Surg.* **90**, 228–229.

THOMAS C. S., CARTER J. W. and LOWDER S. C. (1969) Pericardial tamponade from central venous catheters. *Arch. Surg.* **98**, 217–218.

THOMAS T. V. (1972) Location of catheter tip and its impact on central venous pressure. *Chest* **61**, 668–673.

WARWICK R. and WILLIAMS P. L. (ed.) (1973) *Gray's Anatomy*, 35th ed. London, Longman, p. 700.

WELLMAN K. F., REINHARD A. and SALAZAR E. P. (1968) Polyethylene catheter embolism. *Circulation* **37**, 380–392.

WILSON J. N., GROW J. B., DEMONG C. V., PREVEDEL A. E. and OWENS J. C. (1962) Central venous pressure in optimal blood volume maintenance. *Arch. Surg.* **85**, 55–90.

WISEHEART J. D., HASSAN M. A. and JACKSON J. W. (1972) A complication of percutaneous cannulation of the internal jugular vein. *Thorax* **27**, 496–499.

Br. J. Surg. Vol. 62 (1975) 11–14

The response of the lower oesophageal sphincter to maximal doses of pentagastrin

L. M. TRINDADE, I. L. ROSENBERG, Z. J. ROZYCKI AND G. R. GILES*

SUMMARY

Measurements of the lower oesophageal sphincter pressure and gastric secretion were made in patients with dyspepsia but no reflux and in patients with a hiatus hernia and reflux in response to a near maximal dose of pentagastrin. Patients with hiatus hernia had lower resting sphincter pressures than those with dyspepsia. The magnitude of the pressure rise following pentagastrin was related to the resting tone of the sphincter. However, in terms of percentage increase over resting sphincteric pressure, patients with dyspepsia and patients with a hiatus hernia had similar responses.

IT is still conventional to attribute the symptoms of gastro-oesophageal reflux to the presence of a hiatus hernia. However, there has been considerable scepticism concerning the role of the hiatus hernia in producing these symptoms (Pope, 1970; Cohen and Harris, 1971). Some current views would suggest that the single most important factor in maintaining competence at the cardia and in preventing gastro-oesophageal reflux is the tone and responses of the lower oesophageal sphincter (Castell and Levine, 1971; Cohen and Harris, 1971). This being so, there would be an advantage in developing a reproducible test of sphincteric function which might aid the management of an individual patient. Previous tests of sphincteric function have largely relied upon the pressure changes in the lower oesophageal sphincter in response to mechanical stresses, for example, straight leg raising or from a tight abdominal binder (Lind et al., 1966; Winans and Harris, 1967). More recently, Roszkowski et al. (1973) have investigated the pressure changes of the lower oesophageal sphincter in response to the endogenous gastrin release induced by a test meal stimulus and were able to show diminished responses in patients with gastro-oesophageal reflux. This paper reports an investigation of the responses of the lower oesophageal sphincter and gastric secretory responses to near maximal doses of pentagastrin in patients with dyspepsia or gastro-oesophageal reflux.

Materials and methods

Simultaneous measurement of the lower oesophageal sphincteric pressure and gastric acid secretion was carried out using a multiple tube system. Gastric secretion was aspirated through a size 12 FG plastic tube by continuous suction. Bonded on opposite sides of the nasogastric tube were two fine polyethylene tubes of 1·2 mm internal diameter and 1·4 mm external diameter. One of these fine tubes had a side hole of 1·2 mm diameter at 15 cm from the distal end of the nasogastric tube and the other tube had a similar hole at 20 cm from the distal end (Fig. 1). The fine polyethylene tubes were used for pressure measurement and were perfused continously with normal saline at a rate of 0·6 ml/min. The tubes were connected via pressure transducers to amplified galvanometers, the deflections of which were recorded on ultraviolet-sensitive paper.

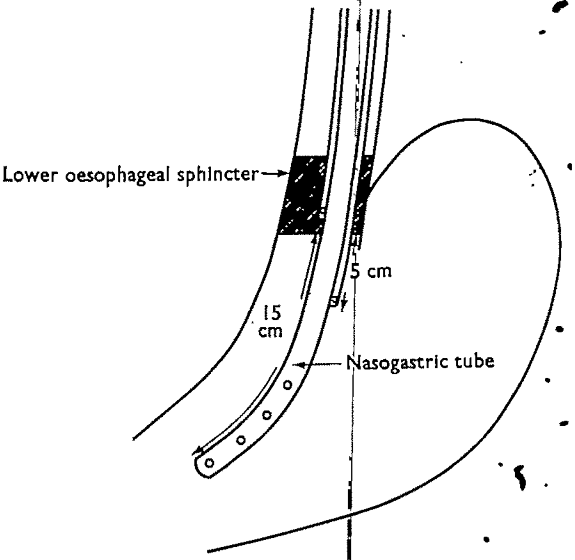


Fig. 1. Position of the manometric tubes in the area of the lower oesophageal sphincter and the gastric fundus. The nasogastric tube is connected to a continuous suction pump for collection of gastric secretion.

After a 12-hour fast the subjects swallowed the tube system into the stomach. The tubes were positioned so that the lowest side hole in the pressure-recording tubes faced the right lateral aspect of the oesophagus. After emptying the stomach of the resting content of gastric juice, the tube system was withdrawn in cm steps with a pressure recording at each interval. This resulted in a pressure profile of the lower oesophageal sphincter, identifying its position with regard to the point of respiratory reversal and the length of amplitude of the sphincteric pressure zone. The tube system was then repositioned so that the upper pressure recording side hole was placed at the point of maximum sphincteric pressure. The lower side hole was situated 5 cm below in the gastric fundus and the aspirating holes of the nasogastric tube 15 cm below in the body of the stomach.

---

* University Department of Surgery, St James's Hospital, Leeds.

Basic gastric secretion was collected for 1 hour in 10-minute aliquots, following which the suction was disconnected and basal sphincteric pressures recorded for 5 minutes. The stomach was again emptied and a deep intramuscular injection of pentagastrin (ICI) given at a dose of 6 μg/kg. Sphincteric pressures were recorded for periods of 2 minutes at 0, 4, 8, 10, 15, 20, 30, 40, 50 and 60 minutes after the injection. In between these periods of pressure recording, gastric secretion was collected in 10-minute aliquots for 1 hour. Simultaneous gastric aspiration and prolonged pressure recordings were not feasible because of the contamination of the gastric samples by the saline perfusing the manometric tubes.

Gastric samples were titrated against 0·1-N sodium hydroxide using Töpfers reagent as an indicator to a pH of 5·6 and the results expressed in terms of concentration (mEq/l) and acid output (mEq/hr). The peak acid output was calculated from the highest two consecutive aliquots collected (Mason and Giles, 1969).

The pressure recordings of the lower oesophageal sphincter were analysed with regard to the sphincteric pressure, and the pressure changes which followed the administration of pentagastrin. All results are expressed in terms of mm Hg.

Combined manometric and gastric secretion studies were carried out on 16 patients with dyspepsia (12 with a duodenal ulcer) and 13 patients with a radiologically demonstrable hiatus hernia. Of the patients with hiatus hernia, 9 were sufficiently symptomatic to warrant surgical repair and the remainder had no symptoms of gastro-oesophageal reflux.

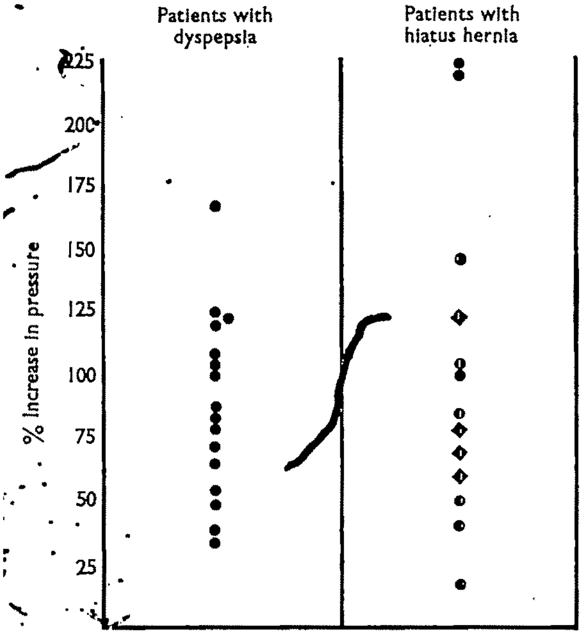


Fig. 2. Maximum percentage increase in the lower oesophageal sphincteric pressure above basal levels after stimulation with pentagastrin 6 μg/kg i.m. The sphincter pressure changes in 4 patients with an asymptomatic hiatus hernia are shown as diamonds.

Results

All the subjects tested were found to have an increase in sphincteric pressure following pentagastrin administration and to show evidence of raised gastric acid output. The peak of the sphincteric pressure response was reached after 8–30 minutes and thereafter declined towards basal levels. This variability in the timing of the pressure peak was assumed to be due to an inconsistent absorption of the intramuscular pentagastrin and bore no relationship to the resting pressures of the lower oesophageal sphincter. However, the peak sphincteric pressure did appear well correlated with the peak of gastric acid output.

1. *Patients with dyspepsia but without hiatus hernia or radiologically diagnosable reflux*

a. Lower oesophageal sphincter pressures: The mean resting sphincter pressure for the 16 patients was 21·6 ± 6·4 mm Hg (range 9·0–34 mm Hg). The mean peak of lower oesophageal sphincter pressure reached 39·6 ± 10·4 mm Hg and ranged from 23·5 to 55·8 mm Hg. The amplitude of the peak lower oesophageal sphincter pressure after pentagastrin was directly related to the resting pressure of the lower oesophageal sphincter ($\gamma = 0{\cdot}8100$, $P < 0{\cdot}001$). In order to allow comparisons between the two groups of patients the peak of the pressure response can be expressed as a percentage change from the resting lower oesophageal sphincter pressure. The mean percentage increase was 87·43 ± 36·3 per cent and individual percentage increases are shown in *Fig.* 2.

Six patients in this group admitted on close questioning to occasional heartburn but without other reflux symptoms. The mean resting pressure for the 6 patients was 20·0 ± 6·3 mm Hg and the mean maximum pressure increase after pentagastrin was also similar to the whole group at 38·2 ± 10·6 mm Hg.

b. Gastric acid secretion: The mean basal acid secretion was 4·64 ± 4·6 mEq/hr, ranging from 0 to 17·3 mEq/hr. The mean peak acid output calculated in the manner described was 39·3 ± 16·5 mEq/hr and ranged from 15·5 to 67·9 mEq/hr. The 6 patients who had heartburn as a symptom appeared to have significantly high mean basal secretion at 8·2 ± 5·6 mEq/hr ($t = 3{\cdot}04$, $P < 0{\cdot}01$) and significantly higher peak acid output at 46·1 ± 17·8 mEq/hr ($t = 3{\cdot}03$, $P < 0{\cdot}01$).

There was no correlation between the resting lower oesophageal sphincter pressures and the basal acid output ($\gamma = 0{\cdot}0201$) or between the maximum lower oesophageal sphincter responses and the peak acid output ($\gamma = 0{\cdot}0503$).

2. *Patients with a symptomatic hiatus hernia and free reflux*

a. Lower oesophageal sphincter pressures: The mean resting pressure of the lower oesophageal sphincter of these 9 patients was 17·9 ± 5·4 mm Hg, ranging from 8·1 to 26·5 mm Hg. This is not significantly different from the patients with dyspepsia ($t = 1{\cdot}42$, $P > 0{\cdot}1$). The mean peak of lower oesophageal sphincter pressure after pentagastrin was 34·1 ± 13·6 mm Hg (range 22–62 mm Hg), which was not significantly different from the patients with dyspepsia ($t = 0{\cdot}87$, $P > 0{\cdot}3$). Finally, the mean percentage increase in lower oesophageal sphincter pressure over the resting pressure was 110·2 ± 79·0 and was extremely variable (*Fig.* 2), ranging from 15 to 23·8 per cent. With this group of patients the peak pressure response of the lower oesophageal sphincter after pentagastrin did not significantly correlate with the resting pressure ($\gamma = 0{\cdot}40$, $P > 70{\cdot}4$).

b. Gastric acid secretion: The mean basal acid output for the group was 5·4 ± 5·4 mEq/hr, ranging from 0·3 to 18·2 mEq/hr. The mean peak acid output was 36·0 ± 22·1 mEq/hr (range 8·1–79·1 mEq/hr). These values clearly do not significantly differ from the group of patients with dyspepsia.

3. *Patients with a hiatus hernia but without reflux*

There were 4 patients in this group and the mean resting lower oesophageal sphincter pressure was 42·0 ± 12·5 mm Hg, ranging from 31 to 60 mm Hg. The peak pressure of the lower oesophageal sphincter after pentagastrin averaged 77·3 ± 24·6 mm Hg (range 55–108 mm Hg). The mean percentage increase in lower oesophageal sphincter pressures was 85·8 ± 23·6 per cent (*Fig.* 2), ranging from 66 to 120 per cent. Since this group was small, worthwhile statistical comparison with the other groups of patients was not possible.

The mean basal secretion of these 4 patients was 4·9 mEq/hr (range 0–9·2 mEq/hr) and the mean peak acid output was 32·9 mEq/hr (range 17·1–47·5 mEq/hr).

Discussion

Gastro-oesophageal competence may depend upon certain anatomico-spatial relationships at the diaphragmatic hiatus and upon the tone of the lower oesophageal sphincter. Whether any of these factors has an overriding importance is debatable, though some workers have suggested that the tone of the lower oesophageal sphincter alone will determine the presence or absence of gastro-oesophageal reflux (Castell and Levine, 1971; Cohen and Harris, 1971). While this may be the position in some cases, it is clear that the majority of patients with reflux have an associated hiatus hernia. Equally, it must be admitted that the tone exerted by the lower oesophageal sphincter may prevent reflux in some patients with hiatus hernia as shown by 4 patients in the present study. It is these inconsistencies which make it advantageous to investigate patients with symptoms of reflux by both manometric and radiological techniques.

The tone of lower oesophageal sphincter under resting conditions has been extensively investigated by techniques which measure the 'squeeze' of the sphincter (Pope, 1967). It has been suggested that resting pressures of less than 10 mm Hg are always associated with reflux (Cohen and Harris, 1971), but this is not the experience of other workers (Haddad, 1970; Brennan et al., 1974). This being so, it seems more appropriate to investigate the reaction of the lower oesophageal sphincter to situations likely to be associated with reflux.

It has been shown that the lower oesophageal sphincter pressure rises during pregnancy (Lind et al., 1968) and in patients with ascites (Simpson and Conn, 1960). The response of the lower oesophageal sphincter to raised intra-abdominal pressure induced by straight leg raising was studied by Lind et al. (1966). Cohen and Harris (1971), using a similar stimulus, were able to show a strong correlation between the occurrence of reflux and a failure of the lower oesophageal sphincter to produce increases in lower oesophageal sphincter pressure which matched the rise in abdominal pressure.

Giles et al. (1969) have shown that the lower oesophageal sphincter pressure is strongly affected by both endogenous and exogenous gastrin. Cohen and Lipschutz (1971) have since demonstrated that the smooth muscle of the lower oesophagus is particularly responsive to circulating gastrin when compared with the muscle layers of the stomach and middle oesophagus. Dose–response curves of the lower oesophageal sphincter to graded intravenous doses of pentagastrin have been constructed and follow a characteristic sigmoid curve (Cohen and Lipschutz, 1971), achieving maximum sphincteric pressure increases of 460 per cent above the resting tone with pure gastrin and 360 per cent above the resting levels with pentagastrin (Lipschutz et al., 1973). Increases of this magnitude were not seen in the present study either in patients with a hiatus hernia or in patients with dyspepsia. These patients are clearly not a control group of normal subjects and thus the responses of the lower oesophageal sphincter may have been altered by their gastro-intestinal disease. However, a more probable explanation is the mode of pentagastrin administration, which in our study was given intramuscularly. Though the dose of 6 μg/kg of pentagastrin intramuscularly has been found to produce near maximal levels of gastric secretion (Johnston and Jepson, 1967; Mason and Giles, 1969) it is probable that serum levels of pentagastrin do not reach the peak concentrations seen after intravenous injections.

The responses of the lower oesophageal sphincter to pentagastrin, in terms of absolute pressure and percentage change, were somewhat higher in the dyspeptic subjects than in the patients with a symptomatic hiatus hernia. However, these differences were not statistically significant and clearly the lower oesophageal sphincter responsiveness to pentagastrin in patients with a hernia approaches normality as judged by this test. The single most important factor in determining the response of the lower oesophageal sphincter to exogenous gastrin would seem to be the resting tone of the sphincter, a point commented upon previously (Cohen and Lipschutz, 1971).

In a study of the lower oesophageal sphincter responses to endogenous gastrin released by a meat extract test meal, Roszkowski et al. (1973) were able to show a clear distinction between patients with symptomatic reflux and control subjects. This distinction has not been paralleled in the present study, where the response to exogenous gastrin by patients with reflux appears normal. Similar findings have been reported by Lipschutz et al. (1973) and have led them to postulate that diminished gastro-oesophageal competence is the result of a diminished release of endogenous gastrin and not necessarily a primary dysfunction of the lower oesophageal sphincter.

Levels of gastric acid secretion in patients with gastro-oesophageal reflux have been variably reported. Some workers have shown gastric hypersecretion (Herrington, 1962; Casten, 1967), while other workers have shown no difference from control subjects (Williams et al., 1967; Silber, 1969). It is probable that high acid secretion in patients with gastro-oesophageal reflux will be found mainly in patients with an associated peptic ulcer.

The values of gastric secretion found in the patients in the present investigation clearly reflect the symptomatology and pathology of the two clinical groups. There does not appear to be any firm correlation between the levels of basal acid secretion and peak acid output and the pressures exerted by the lower oesophageal sphincter. However, studies of gastric acid secretion in patients with a hiatus hernia may be of assistance to surgeons, in order that the surgical repair can be supplemented where necessary by a procedure which will reduce the acid secretion. Studies using a combined test of manometry and gastric secretion are thus potentially of clinical value. However, since the use of pentagastrin does not readily distinguish lower oesophageal spincter dysfunction in patients with reflux, it will be necessary to continue the use of a test meal system. In practical terms, failure of the lower oesophageal sphincter to respond to either form of stimulus should warn the surgeon that simple hiatus hernia repair may not be successful and indicates the need for some form of surgical reconstruction at the cardia.

References

BRENNAN T. G., TRINDADE L. M., ROZYCKI Z. J. and GILES G. R. (1974) The influence of the lower oesophageal sphincter pressure on the outcome of hiatus hernia repair. *Br. J. Surg.* **61**, 201–205.

CASTELL D. O. and LEVINE S. M. (1971) Lower esophageal sphincter response to gastric alkalinisation. *Ann. Intern. Med.* **74**, 223–227.

CASTEN D. F. (1967) Peptic oesophagitis, hiatal hernia and duodenal ulcer. *Am. J. Surg.* **113**, 638–642.

COHEN S. and HARRIS L. D. (1971) Does hiatus hernia affect competence of the gastro-oesophageal sphincter? *New Engl. J. Med.* **284**, 1053–1057.

COHEN S. and LIPSCHUTZ W. (1971) Hormonal regulation of human lower oesophageal sphincter competence: interaction of gastrin and secretin. *J. Clin. Invest.* **50**, 449–454.

GILES G. R., MASON M. C., HUMPHRIES C. and CLARK C. G. (1969) The action of gastrin on the lower oesophageal sphincter in man. *Gut* **10**, 730–735.

HADDAD J. K. (1970) Relation of gastro-esophageal reflux to yield sphincter pressures. *Gastroenterology* **58**, 175–185.

HERRINGTON J. L. (1962) The treatment of esophageal hiatal hernia. *Arch. Surg.* **89**, 379–387.

JOHNSTON D. and JEPSON K. (1967) Use of pentagastrin in a test of gastric acid secretion. *Lancet* **2**, 585–588.

LIND J. F., SMITH A. M. and MCIVER D. K. (1968) Heartburn in pregnancy—a manometric study. *Can. Med. Assoc. J.* **98**, 571–574.

LIND J. F., WARRIAN W. G. and WANKLING W. J. (1966) Responses of the gastro-oesophageal junctional zone to increases in intra-abdominal pressure. *Can. J. Surg.* **9**, 32–38.

LIPSCHUTZ W. H., GASKINS R. D., KINKASH W. M. and SODE J. (1973) Lower esophageal sphincter incompetence. *New Engl. J. Med.* **289**, 182–184.

MASON M. C. and GILES G. R. (1969) The gastrin test: an evaluation and simple modification. *Gut* **9**, 375–378.

POPE C. G. (1967) A dynamic test of sphincter strength: its application to the lower oesophageal sphincter. *Gastroenterology* **52**, 779–786.

POPE C. G. (1970) The esophagus: 1967 to 1969. *Gastroenterology* **59**, 460–475.

ROSZKOWSKI A., GUILLOU P. and GILES G. R. (1973) The response of the lower oesophageal sphincter to a test-meal stimulus. *Br. J. Surg.* **60**, 489–493.

SILBER W. (1969) Augmented histamine test in the treatment of symptomatic hiatal hernia. *Gut* **10**, 611–615.

SIMPSON J. A. and CONN H. O. (1960) Role of ascites in gastro-oesophageal reflux with comments on the pathogenesis of bleeding oesophageal varices. *Gastroenterology* **55**, 17–24.

WILLIAMS C. B., LAWRIE J. H. and FORREST A. P. M. (1967) Acid secretion in symptomatic sliding hiatus hernia. *Lancet* **1**, 182–184.

WINANS C. S. and HARRIS L. D. (1967) Quantitation of lower esophageal sphincter competence. *Gastroenterology* **52**, 773–778.

Br. J. Surg. Vol. 62 (1975) 15–18

Relationship between changes in plasma gastrin and lower oesophageal sphincter pressure after meals

I. W. McCALL, R. F. HARVEY, CAROLINE J. OWENS AND B. G. CLENDINNEN*

SUMMARY

Changes in plasma gastrin and lower oesophageal sphincter pressure were measured in 20 subjects after a standard protein meal. Significant increases in both gastrin and sphincter pressure were seen. Peak gastrin response occurred an average of 19·5 minutes and peak lower oesophageal sphincter response 43·0 minutes after the meal. Both gastrin and sphincter pressure showed a wide spectrum of response. In 5 subjects there was no appreciable rise (< 5 pg/ml) in plasma gastrin after the meal, and 3 of these had symptoms of oesophageal reflux. In this group there was only a small but nevertheless significant rise in lower oesophageal sphincter pressure (mean pressure rise 18·0 per cent of fasting value, $P < 0.05$). Greater increases in sphincter pressure (mean rise 54·2 per cent, $P < 0.005$) were seen in subjects with a moderate (up to 50 pg/ml) rise in plasma gastrin, and those with the most marked gastrin response (> 50 pg/ml) showed the greatest rise in pressure (mean rise 80·3 per cent, $P < 0.0025$).

These results suggest that endogenous plasma gastrin is the main stimulus to the rise in lower oesophageal sphincter pressure after food. Subjects with a poor gastrin response to the meal have only a small increase in sphincter pressure and as a result may be more liable to develop gastro-oesophageal reflux.

REFLUX of gastrin contents into the oesophagus is normally prevented by a high pressure zone (the lower oesophageal sphincter) at the gastro-oesophageal junction (Pope, 1967; Winans and Harris, 1967; Cohen and Harris, 1970). After meals there is an increase in lower oesophageal sphincter pressure (Giles et al., 1969; Castell and Harris, 1970; Nebel and Castell, 1972). Similar increases are seen after intravenous injections of pentagastrin and gastrin (Giles et al., 1969; Cohen and Lipshutz, 1971), indicating that endogenous gastrin may be responsible for the increased sphincter pressure after food. Acidification of a meal (which inhibits endogenous gastrin release) prevents the usual pressure rise (Nebel and Castell, 1972).

Lipshutz et al. (1973) demonstrated that subjects with symptomatic gastro-oesophageal reflux have an abnormally small increase in lower oesophageal sphincter pressure after food when compared with control subjects, whereas the response of the sphincter to injected pentagastrin is normal. This suggests that incompetence of the lower oesophageal sphincter might be due to a defect in the release of endogenous gastrin. In order to test this hypothesis we have measured and compared the changes in lower oesophageal sphincter pressure with direct measurements of endogenous plasma gastrin after a standard protein meal.

Materials and methods

Changes in lower oesophageal sphincter pressure and endogenous plasma gastrin after a standard meat extract meal were measured in 20 volunteers (9 normal subjects, 8 generally well patients with no evidence of gastro-intestinal disease who were convalescing from minor surgical operations and 3 patients with symptomatic gastro-oesophageal reflux). All the subjects had fasted for at least 6 hours before the test.

Lower oesophageal sphincter pressures were measured by using catheters of 1·2 mm internal diameter constantly perfused with 1·0 ml/minute of water and connected to a Devices M19 recording system. The tubes were passed into the stomach, then slowly withdrawn through the sphincter, this resulting in a pressure profile (*Fig.* 1). The figure taken was the difference between the maximum sphincter pressure and the pressure in the gastric fundus. The fasting level was taken from the mean of three readings and all subsequent values were expressed as a percentage of this fasting level.

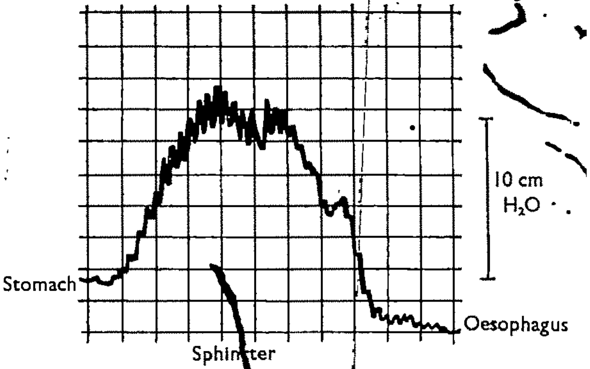


Fig. 1. Pressure 'profile' obtained by withdrawing the pressure-recording catheter slowly from the stomach to the oesophagus.

Venous blood samples for gastrin estimation were taken from an indwelling catheter and the plasma separated within 2 hours and frozen at −20 °C until assayed. A radio-immunoassay with double-antibody separation was employed (Jackson et al., 1972), using a rabbit antibody to synthetic human gastrin 1

---

* University Departments of Radiology, Medicine and Surgery, The Royal Infirmary, Bristol BS2 8HW.

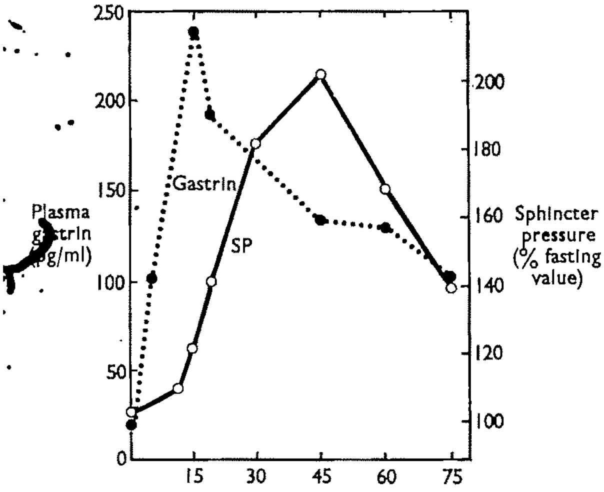


Fig. 2. Changes in sphincter pressure and plasma gastrin after the test meal in a single subject.

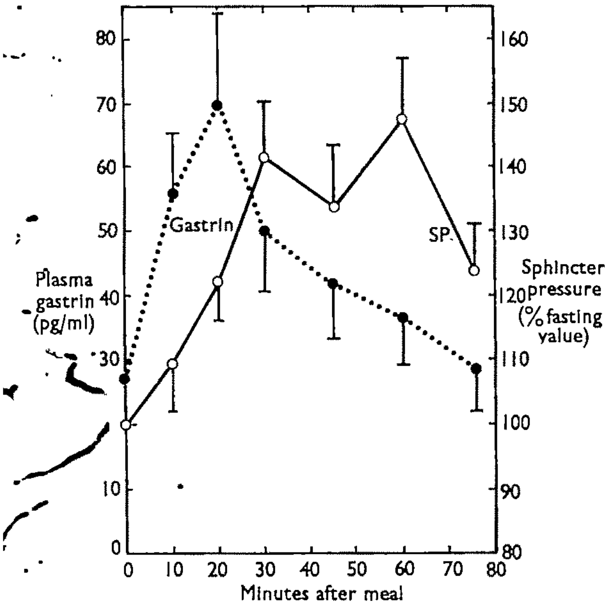


Fig. 3. Changes in sphincter pressure and plasma gastrin after the test meal (all subjects). Mean values and standard errors are shown.

(residues 2–17). All the samples were assayed in triplicate, the mean of the triplicates being taken as the serum gastrin level. Intra-assay variation was less than 10 per cent and interassay variation up to 15 per cent. The lower limit of sensitivity of the assay was 10 pg/ml of plasma.

After taking the fasting pressure measurements and fasting blood for gastrin estimation, all the subjects drank a standard meal consisting of 8·0 g of meat extract (Bovril) dissolved in 300 ml water buffered to pH 7·0 with approximately 1·0 g TRIS (hydroxymethyl) aminomethane (Sigma). Measurements of lower oesophageal sphincter pressure and samples for plasma gastrin were then obtained 5, 10, 15, 20, 30, 45, 60 and 75 minutes after this meal.

Results

Following the test meal there were significant increases in both plasma gastrin (from a mean fasting level of 27·3 ± 6·8 (s.e.) to a peak of 74·4 ± 13·7 pg/ml, $P < 0·005$) and in lower oesophageal sphincter pressure (mean increase 53·0 ± 9·4 per cent of fasting value, $P < 0·001$). The maximal mean rise in plasma gastrin occurred within 20 minutes of taking the Bovril in all but 3 subjects (mean 19·5 ± 2·4 minutes), but the maximal mean response of the lower oesophageal sphincter pressure occurred some time later (mean 43·0 ± 4·1 minutes after the Bovril). The changes for the subjects with the greatest gastrin rise and for the whole group are shown in *Figs.* 2 and 3 respectively.

The response to the meal of both the plasma gastrin and lower oesophageal sphincter pressure varied widely. In a group of 5 subjects in whom plasma gastrin levels did not change appreciably (mean levels 43·0 ± 23·7 pg/ml fasting, 43·6 ± 22·1 pg/ml postprandial, maximum increase 4 pg/ml) there was only a small though significant rise in lower oesophageal sphincter pressure (18·0 ± 8·2 per cent, $P < 0·05$). This was considerably less than that seen in subjects with a significant rise in plasma gastrin in whom the oesophageal sphincter showed a peak rise of pressure of 64·7 ± 10·7 per cent ($P < 0·025$). In order to analyse the results in more detail the subjects showing a significant gastrin response were divided into two further groups (*Table I*). Those with a moderate rise of 19–50 pg (9 subjects) showed a more marked pressure increase of 54·2 ± 14·2 per cent than those with no gastrin response, and subjects with rises in

Table I: CHANGES IN GASTRIN AND SPHINCTER PRESSURE AFTER A TEST MEAL

Group	No. of subjects	Fasting gastrin (pg/ml)	Peak gastrin (pg/ml)	Increase in gastrin (pg/ml)	Rise in sphincter pressure (%)
No significant (<5 pg/ml) rise in gastrin after the meal	5†	43·0±23·7	43·6±22·1	0·6± 1·7*	18·0± 8·2**
Moderate (19–50 pg/ml) rise in gastrin after the meal	9	16·4± 1·8	49·1± 3·2	32·7± 3·4****	54·2±14·2***
Marked (>50 pg/ml) rise in gastrin after the meal	6	30·3±11·4	137·8±29·3	107·5±27·5***	80·3±15·2***
All subjects	20	27·3± 6·8	74·4±13·7	47·1±12·2***	53·0± 9·4****

* Not significant, **$P = 0·05$, *** $P = 0·01$, **** $P = 0·001$.
† Including 3 patients with symptomatic gastro-oesophageal reflux.

gastrin levels of more than 50 pg/ml showed an even more striking increase in lower oesophageal sphincter pressure (mean 80·3 ± 15·2 per cent).

The correlation between peak gastrin rise and peak lower oesophageal sphincter pressure rise in individual subjects did not quite reach significant levels ($r = 0{\cdot}37$, $n = 20$, $0{\cdot}05 < P < 0{\cdot}10$). However, when the 2 subjects with the greatest rises in gastrin (157 and 221 pg/ml) were excluded the correlation was significant ($r = 0{\cdot}52$, $n = 18$, $P < 0{\cdot}05$). This may indicate that the relationship between peak pressure response and peak rise in plasma gastrin is not strictly a linear one.

The 3 patients with symptomatic gastro-oesophageal reflux were all in the group of 5 subjects who showed no increase in plasma gastrin and little rise in sphincter pressure after the meal.

Discussion

The lower oesophageal sphincter is known to be a major factor in the prevention of gastro-oesophageal reflux (Pope, 1967; Winans and Harris, 1967; Cohen and Harris, 1970), and sphincter pressure may be more important than the exact location of the gastro-oesophageal junction, suggesting that a simple positional change, as seen with hiatus hernia, is not the cause of gastro-oesophageal reflux (Cohen and Harris, 1971). It has recently been confirmed that patients with symptomatic gastro-oesophageal reflux have a smaller sphincter pressure than do control subjects, both basally and also after standard stimuli (e.g. intragastric alkali and glycine) (Lipshutz et al., 1973).

The role of gastrin in maintaining lower oesophageal sphincter strength is now well established (Giles et al., 1969; Castell and Harris, 1970; Cohen and Lipshutz, 1971; Lipshutz et al., 1972), and it follows that gastro-oesophageal hypotension and incompetence might be due to some defect in the action of gastrin on the lower oesophageal sphincter. There are several possible ways in which this might come about. The sphincter in patients with reflux might in some way be inherently abnormal. However, patients with symptomatic reflux show a similar sphincter response to direct muscle stimulation by a parasympathomimetic drug (bethanechol chloride) and a cholinesterase inhibitor (edrophoninum chloride) to control subjects (Lipshutz et al., 1973). The sphincter might be inherently normal but for some reason resistant to the action of gastrin. However, dose–response curves of lower oesophageal sphincter pressure to exogenous intravenous pentagastrin obtained by these same workers were similar in patients with reflux and in controls. The third possibility is that the sphincter of the patient with reflux receives an inadequate stimulus to contract. In support of this theory Lipshutz and his colleagues (1973) have shown that in such patients the pressure response of the sphincter to oral stimuli designed to release endogenous gastrin is reduced. Our finding that the pressure response of the lower oesophageal sphincter is proportional to the gastrin response after a meal in the majority of subjects supports this hypothesis. Of the 5 subjects showing no appreciable rise in plasma gastrin in response to the meal, 3 had symptomatic gastro-oesophageal reflux.

It is of interest that the 5 subjects who did not show a rise in serum gastrin after the meal nevertheless showed a small but significant increase in lower oesophageal sphincter pressure (*Table I*). This indicates that although gastrin may be the main stimulus to the rise in sphincter pressure after food, it is not the only one. Other nervous or hormonal factors may have some importance in subjects who for some reason do not show a normal endogenous gastrin response.

The time lag between the peak endogenous serum gastrin concentration and the peak increase in lower oesophageal sphincter pressure is also of interest, and we are not aware that it has been reported previously. A degree of delay might be expected, as gastrin in blood is presumably not active until it has come into contact with and become bound by specific receptors on the cells of the target tissue. Little is known of this process in the case of gastrin.

Our results, taken in conjunction with those of previous workers, suggest that gastro-oesophageal hypotension and associated incompetence may be due to a defect in endogenous gastrin release by the stomach. If confirmed, this might have important therapeutic implications in the management of patients with gastro-oesophageal reflux.

Acknowledgements

The generous gift of antigastrin antibodies by Dr J. C. Thompson, USA, is gratefully acknowledged. We also thank the volunteers who took part in the study and physicians and surgeons of the United Bristol Hospitals who allowed us to study their patients. This work was supported in part by the Medical Research Council.

References

CASTELL D. O. and HARRIS L. D. (1970) Hormonal control of gastro-esophageal sphincter strength. *New Engl. J. Med.* **282**, 886–889.

COHEN S. and HARRIS L. D. (1970) Lower esophageal sphincter pressure as an index of lower esophageal sphincter strength. *Gastroenterology* **58**, 157–162.

COHEN S. and HARRIS L. D. (1971) Does hiatus hernia affect competence of the gastroesophageal sphincter? *New Engl. J. Med.* **284**, 1053–1056.

COHEN S. and LIPSHUTZ W. (1971) Hormonal regulation of human lower esophageal sphincter competence: interaction of gastrin and secretin. *J. Clin. Invest.* **50**, 449–454.

GILES G. R., MASON M. C., HUMPHRIES C. and CLARK C. G. (1969) Action of gastrin on the lower oesophageal sphincter in man. *Gut* **10**, 730–734.

JACKSON B. M., REEDER, D. D. and THOMPSON J. C. (1972) Dynamic characteristics of gastrin release. *Am. J. Surg.* **123**, 137–142.

LIPSHUTZ W. H., GASKINS R. D., LUKASH W. M. and SODE J. (1973) Pathogenesis of lower esophageal sphincter incompetence. *New Engl. J. Med.* **289**, 182–184.

LIPSHUTZ W. H., HUGHES W. and COHEN S. (1972) The genesis of lower esophageal sphincter pressure: its identification through the use of gastrin antiserum. *J. Clin. Invest.* **51**, 522–529.

NEBEL O. T. and CASTELL D. O. (1972) Lower esophageal sphincter pressure changes after food ingestion. *Gastroenterology* **63**, 778–783.

POPE C. E. (1967) A dynamic test of sphincter strength: its application to the lower esophageal sphincter. *Gastroenterology* **52**, 779–786.

WINANS C. S. and HARRIS L. D. (1967) Quantitation of lower esophageal sphincter competence. *Gastroenterology* **52**, 773–778.

Circumstances and accidents, such as I have related, rendered it very difficult however to procure good qualified surgeons for the army, and a curious expedient was resorted to in consequence. Political economists say that when the demand for tea, coffee, sugar, cotton, &c. &c. is greater than the supply, the price will increase, and that human labour ought to be regulated by the same rule; the authorities in England thought however otherwise, and instead of increasing the price, or smoothing away the difficulties, they deteriorated the article, and as surgeons could not be found qualified to kill or cure by commission, they thought it right to take those of an inferior description, and give them only a warrant, as they do to boatswains and gunners on board-ship. I do not know whether this bright idea originated with the Government or the Army Medical Board; but when elicited, it seemed to please all parties, and a certain number of gentlemen thus warranted to do business came out to Spain. I had some of them at San Andero, where I was for a couple of months. One poor fellow having called to report his arrival, I desired him to sign a paper descriptive of his qualifications. This I found he could scarcely do, the letters very much resembling pot-hooks; which he attributed to sea-sickness, in which I sympathized with him, my own stomach being easily unshipped by a very moderate view of blue salt water. I therefore sent him to live at one of the fever-hospitals, to do duty for a few days, until I might see what he was made of.

G. J. GUTHRIE FRS (1838) *Clinical Lectures . . . on the Diseases of the Peninsula* . . . London, Churchill.

Br. J. Surg. Vol. 62 (1975) 19–22

A survey of the results of the Boerema anterior gastropexy for hiatus hernia over a 4-year period

C. J. DAVIES*

SUMMARY

The results obtained by using the Boerema anterior gastropexy for symptomatic hiatus hernia over a 4-year period are reviewed. All 68 patients were operated upon by the same surgeon. The success rate as judged by relief of the patients' symptoms was 90 per cent.

It is felt that the operation has advantages such as to justify its wide use.

IN 1972 the results were published of 101 operations for symptomatic hiatus hernia (Magary, 1972). All the operations had been done in Bath by the same surgeon. It emerged from this comparison of methods of repair that the Boerema anterior gastropexy had significantly less clinical failures. It also had the merit of being simple and could be performed quickly. For these reasons the Boerema procedure gained preference, and it has been used exclusively since 1970 by the surgeon concerned (Mr H. T. John, Consultant Surgeon, Bath Clinical Area). The results of this procedure over a 4-year period have now been reviewed.

Materials and methods

In the years 1968–72, 72 patients underwent a Boerema repair for symptomatic hiatus hernia confirmed by radiology and/or oesophagoscopy. A questionnaire was sent to each patient; 3 did not reply and 1 questionnaire was returned marked 'Gone away', leaving 68 patients available for this survey.

An analysis of these patients according to sex and age (*Table I*) shows that 47 out of the 68 patients (nearly 70 per cent) are over 50 years old, females outnumber males by more than 2 to 1 and half the patients are females over the age of 50.

Examination of the case notes showed that 6 patients had undergone previous surgery for hiatus hernia. The details of these and other relevant operations are given in *Table II*.

At laparotomy it was common to find pathology as well as the hiatus hernia (*Table III*), and several operative procedures were carried out in addition to the Boerema repair (*Table IV*).

Magary (1972) used a system of grading of severity of symptoms due to hiatus hernia (*Table V*) and this has been adhered to. The patients were sent a questionnaire which was framed in such a way that the patients themselves selected the grade into which their symptoms fell. In an attempt to isolate the symptoms related to hiatus hernia and gastro-oesophageal reflux, they were asked also to state whether any symptoms they had were the same as or different from those of which they complained preoperatively. In addition, they were asked to describe their symptoms.

The preoperative grading of symptoms (*Table VI*) was done by reference to the referral letter and the outpatient and inpatient case histories. Postoperative gradings were made from the case notes, data from a previous survey involving 39 of these patients (Magary, 1972) and the questionnaire for the present study to assess the current state of the patients' health. The patients undergoing surgery with grade 2 symptoms usually had some other feature, such as gastrointestinal bleeding; 88 per cent of the patients had severe grade 3 or 4 symptoms.

Operation

A full description of the technique of the anterior gastropexy has been given elsewhere (Boerema, 1969). Essentially, it involves reduction of the stomach and lower oesophagus into the abdomen aided by freeing of the vagi and the oesophagus from all surrounding structures by blunt dissection. Approximation of the two limbs of the right crus behind the oesophagus is optional. The gastropexy itself consists of approximating the anterior wall of the stomach 0·5 cm below the lesser curve to the linea alba using five or six nonabsorbable sutures. The intention is to take up the slack of the lesser curve so that ultimately the intra-abdominal oesophagus and the upper part of the lesser curve feel like a very tense cord extending from the hiatus close along the undersurface of the liver to the anterior abdominal wall 2·5 cm to the right of the midline.

Results

Mortality

Three patients died in the immediate postoperative period. These deaths were due to myocardial infarction in a man aged 59, pulmonary embolus in a man aged 83 and a combination of bronchopneumonia, subphrenic abscess and wound dehiscence in a man aged 64. The latter patient had undergone an operation for repair of hiatus hernia 5 years previously, and during the mobilization prior to performing the gastropexy his oesophagus was torn and resutured. This was the only immediate postoperative death that could be attributed to the nature of this operation rather than to the hazards of surgery and anaesthesia in general. However, the 3 deaths together give a perioperative mortality of 4·4 per cent. A further patient died

---

* Surgical Registrar, Bath Group of Hospitals.
Present address: Manchester Royal Infirmary.

Table I: ANALYSIS OF 68 PATIENTS BY AGE AND SEX

	Age (yr)							Total	
Sex	21–30	31–40	41–50	51–60	61–70	71–80	81–90	No.	(%)
Females	1	3	10	10	16	8	0	48	71
Males	1	1	5	9	3	0	1	20	29
Total	2	4	15	19	19	8	1	68	100

Table II: PREVIOUS RELEVANT OPERATIONS

Operation:	No. of cases:
Transthoracic repair of hiatus hernia	5
Other repair of hiatus hernia (not Boerema)	1
Cholecystectomy	6
Partial gastrectomy	2
Vagotomy and pyloroplasty	1

Table III: FINDINGS AT OPERATION OTHER THAN HIATUS HERNIA

Findings:	No. of cases:
Gallstones	6
Duodenal ulcer	4
Diverticular disease	3
Benign oesophageal stricture	2
Achalasia of the cardia	1
Stones in common bile duct	1
Duodenal diverticulum	1
Thickened appendix	1
Meckel's diverticulum	1
Cyst of kidney	1
Adhesions ? cause	1

Table IV: OPERATIVE PROCEDURES IN ADDITION TO THE BOEREMA REPAIR

Operation:	No. of cases:
Cholecystectomy	6
Vagotomy and pyloroplasty	4
Splenectomy	2
Heller's operation	1
Duodenal diverticulectomy	1
Appendicectomy	1
Diagnostic thoracotomy	1
Suture ruptured oesophagus	1
Exploration of common bile duct and removal of stone	1
Liver biopsy (for jaundice)	1

Table V: GRADING OF CLINICAL SYMPTOMS*

Grade	Severity	Description
1	Absent	No symptoms
2	Mild	Symptoms usually relieved by conservative measures
3	Severe	Symptoms resistant to conservative measures
4	Severe	Persistent incapacitating symptoms

* Related to the hiatus hernia or resulting from operation.

Table VI: PREOPERATIVE SYMPTOMS

Grade	No. of cases	%
1	0	—
2	8	12
3	52	76
4	8	12
Total	68	100

Table VII: COMPLICATIONS

		No. of cases:
Immediate:	Wound infection	6
	Burst abdomen	2
	Chest infection	3
	Subphrenic abscess	1
	Pneumothorax	1
	Ileus	1
	Dysphagia	2
	Vomiting	1
Late:	Postvagotomy dumping	1
	Incisional hernia	4
	Wound pain	5

Table VIII: POSTOPERATIVE SYMPTOMS

	Length of follo[illegible]					
Grade*	0–½ yr	½–1 yr	1–2 yr	2–3 yr	3–4 yr	4 yr+
1	66·25	53	42	43	50	38
2	26·25	39	47	52	44·5	54
3	6	6·5	9	5	5·5	8
4	1·5	1·5	2	0	0	0
1 and 2	92·5	92	89	95	94·5	92
No. of patients	65	62	57	42	18	13

* Results shown as percentage of patients in each grade.

Table IX: CURRENT SYMPTOMS

Initial grading	No. of patients	Final grading*			
		1	2	3	4
1	—	—	—	—	—
2	6	5	1	—	—
3	49	21	22	5	1
4	8	3	4	1	—

* At time of survey, therefore including patients at various postoperative intervals.

6 months after the original operation, the cause of death being bronchopneumonia and upper gastrointestinal haemorrhage following oesophagoscopy and insertion of a Celestin tube for oesophageal stricture. It was felt at the second operation that the stricture may have been neoplastic, but no biopsy was taken and post-mortem examination was not performed. Her case was included in the analysis at 0–6 months, as she was seen 5 months postoperatively with grade 3 dysphagia. A fifth patient died of causes unrelated to her hiatus hernia repair 12 months postoperatively.

Morbidity

It was common to get minor degrees of dysphagia for the first 4–6 weeks but this symptom nearly always disappeared spontaneously and patients could be confidently reassured on this point. Apart from the cases of pneumothorax, dysphagia and vomiting, the immediate complications (*Table VII*) were not specific to the operation. The incidence of incisional hernias is undoubtedly related to the relative weakness of a midline incision associated with wound sepsis. One patient reacted against the thread sutures and underwent several explorations of wound sinuses.

Follow-up

At the time of the review the length of follow-up ranged from less than 6 months to more than 4 years. Obviously the numbers of patients available for review decreased with a lengthening postoperative time interval. Not all the available patients were seen at each time interval as most had been discharged from the outpatients' department soon after their operation. In some cases it was possible to fill in the correct grading of symptoms from details on the *pro formas* of the previous survey (Magary, 1972). When this was not possible the grade of symptoms at a particular time interval has been extrapolated from prior or later information, the worse grading of the two possibilities being assumed. Thus, if a patient seen in the clinic between 6 and 12 months was thought to have mild grade 2 symptoms and then the next contact was through the questionnaire at 2–3 years when the patient admitted to no symptoms (grade 1), it would be assumed for this survey that for the intervening time interval of 1–2 years he would have had grade 2 rather than grade 1 symptoms.

The results of these facts and assumptions are shown in *Table VIII*. It can be seen that up to 6 months postoperatively two-thirds of patients are completely symptom-free (grade 1), but that over the years this number drops to around 40 per cent. If, however, the patients with mild grade 2 symptoms (e.g. 'mild heartburn', 'mild indigestion', 'occasional slight nausea') are grouped with those with no symptoms, the numbers stay steady at around 90 per cent. This carries with it, of course, the corollary of a 10 per cent failure rate, i.e. those with severe grade 3 or 4 symptoms. Many patients with grade 2 symptoms also wrote of their own accord that they were grateful for the improvement in their wellbeing, and that they regarded the operation as a success. Only one patient claimed to have grade 4 symptoms and she had been noted preoperatively to be an unhappy woman (probably with just cause) with a strong functional overlay.

The current state of the patients' symptoms was assessed with regard to the grading of their initial symptoms (*Table IX*). This analysis obviously involved only the 63 patients alive at the time of the survey. Six patients said they were no better off, and one claimed to be worse off than before operation.

It should be said that the surgeon operating on all these patients has not participated in the analysis of the results and so in that sense they are presented by a disinterested person.

Discussion

Boerema first performed his operation of anterior gastropexy in 1952 and several reports of his cases have appeared since then. He devised the operation as he became dissatisfied with his own high recurrence rate in hernias repaired through both the chest and the abdomen. There is difficulty, of course, in deciding what constitutes a recurrence, for about 25 per cent of the anatomically good results are no success clinically, and about 25 per cent of patients who are symptom-free show an anatomical recurrence (Boerema, 1969). In the present survey the presence or absence of symptoms has been the factor determining success or failure, for it is in these terms alone that the patient judges whether or not an operation has been worth while.

A recent historical review of surgery for hiatus hernia (Mullard, 1971) shows how early emphasis on the anatomical defect and therefore the necessity for an anatomical repair, as advocated by Harrington (1940) and Allison (1951), gave way to a more physiological approach concentrating on the prevention of gastro-oesophageal reflux. The concept of the right crus carrying responsibility for maintaining the sphincter and preventing reflux was important in this new approach (Belsey, 1954). Boerema, however, rejects this theory, finding it unlikely that prevention of gastric reflux depends upon a muscular arch not situated at the oesophagogastric junction.

In his dissatisfaction with the results of repairing hiatus hernias by narrowing the hiatus and fixing the oesophagus to the diaphragm, Boerema, initially concerned only with preventing the upward herniation of the stomach, concentrated on a third principle: fixation of the stomach from below, and attached the stomach to the best available structure—the anterior abdominal wall. He was then struck by the constant absence of reflux, the longer length of intra-abdominal oesophagus resulting from anterior gastropexy never becoming the seat of postoperative oesophagitis. He concluded that the crural sling played no part in controlling reflux and so directed his attention to the oesophagogastric junction.

He postulated that the angle formed by the long axes of the oesophagus and the lesser curve of the stomach was of paramount importance. The more nearly parallel these axes were, the less likely was it that regurgitation would occur. The mechanism responsible for maintaining this angle acute was not the fixed sling of the crura but a mobile sling formed by intrinsic gastric musculature, beginning distally on the lesser curve, ascending up the cardia, splitting to pass in front of and behind the oesophagogastric junction and rejoining in the cardiac notch. He likened this sling to a tennis racket, the head around the lower oesophagus and the handle along the lesser curve. Pulling the handle down would accentuate the oblique entrance of the oesophagus into the stomach, thus preventing reflux. Boerema maintained that the mobile sling did just this in life, pulling from the fixed point of the retroperitoneal duodenum. Attaching the lesser curve of the stomach to the anterior abdominal wall under tension would have exactly the same effect on the oesophagogastric angle and so on the prevention of reflux.

Two problems should be mentioned with respect to this survey. First, although much data was obtained from the case notes, information concerning the latest condition of the patients was obtained by means of a postal questionnaire. As always, this has problems of imprecision. The questionnaire was designed, however, to eliminate this as far as possible.

P 25 354

and one was impressed with the care with which the majority of patients filled it in. Possibly this was some reward for its brevity. Only four specific questions were asked. Space was provided for additional comments. In this way some separation of the factual from the emotional response was achieved. Secondly, in common with other authors (Zuidema, 1972) a high proportion (32 per cent in this survey) of patients had additional intra-abdominal pathology (*Table III*), most of which was dealt with at the same time as the gastropexy (*Table VI*). Again this makes for difficulties in assessing the significance of symptoms reported by the patients. This difficulty is acknowledged and has been catered for to a certain extent by asking the patients for an exact description of their symptoms. These were then assessed and categorized by the author. For example, postoperative symptoms such as heartburn and dysphagia were regarded as being associated with hiatus hernia and reflux, whereas postprandial distension after gastropexy and vagotomy seemed more likely to be due to the latter. In view of these problems, however, it is recognized that the findings of this survey should be interpreted with some caution.

In comparison with Boerema's review of 500 cases, giving a mortality rate of 1 per cent and a recurrence rate of 5 per cent (Boerema, 1969), the present survey is a modest one. Nevertheless, it has value in that it presents the results obtained by a surgeon who has learnt the technique from its originator, found that the operation works (Magary, 1972) and has therefore continued to use it. Up to now, the technique and the results obtained with it by Boerema have met with only mild interest in this country. It is felt that a greater interest is now beginning to be shown and the publication of results obtained here may encourage other surgeons to try it out, particularly if they are dissatisfied with their own results using other techniques. The main advantage of the Boerema anterior gastropexy are that it has a 90 per cent success rate and that it can be performed quickly (about 45 minutes) and safely.

Acknowledgements

I would like to thank Mr H. T. John for his permission to study the patients under his care, the patients themselves for their willingness and care in replying to the questionnaire and Miss Joan Sellick and Miss Susan Davies for invaluable secretarial assistance.

References

ALLISON P. R. (1951) Reflux oesophagitis, sliding hiatal hernia, and the anatomy of repair. *Surg. Gynecol. Obstet.* **92**, 419–431.

BELSEY R. H. R. (1954) Peptic ulcer of the oesophagus. *Ann. R. Coll. Surg.* **14**, 303–322.

BOEREMA I. (1969) Hiatus hernia: repair by right-sided, subhepatic, anterior gastropexy. *Surgery* **65**, 884–893.

HARRINGTON S. W. (1940) Diagnosis and treatment of various types of diaphragmatic hernia. *Am. J. Surg.* **50**, 381–446.

MAGARY C. J. (1972) The results of 101 operations for symptomatic hiatus hernia: a comparison of two different methods. *Br. J. Surg.* **59**, 432–436.

MULLARD K. S. (1972) The surgical treatment of diaphragmatic oesophageal hiatus hernia. *Ann. R. Coll. Surg.* **50**, 73–91.

ZUIDEMA G. D. (1972) Surgical treatment: abdominal approach. In: SKINNER D. B., BELSEY R. H. A., HENDRIX T. R. and ZUIDEMA G. D. (ed.) *Gastro-oesophageal Reflux and Hiatal Hernia.* Boston, Little, Brown, pp. 151–161.

Br. J. Surg. Vol. 62 (1975) 23-25

Atrophic gastritis in gastrectomy specimens

J. M. SKINNER, P. J. HEENAN AND R. WHITEHEAD*

SUMMARY

Examination of gastrectomy specimens has shown that atrophic gastritis and intestinal metaplasia are widespread and have the same distribution in cancer of the stomach as in gastric ulcer affecting the body. Their distribution is restricted to the distal part of the stomach in pyloric ulcer. After gastrojejunostomy the distribution is also like that seen in cancer. There is a close association of widespread atrophic gastritis and intestinal metaplasia with the development of cancer and a higher cancer rate after stomach operation for benign conditions. The similarity of distribution of atrophic gastritis and intestinal metaplasia in the stomach with body ulcer to that in cancer and after gastrojejunostomy points to a higher cancer risk in the stomach containing a body ulcer.

IT has been shown by Stalsberg and Taksdal (1971) that 15 years after patients have been operated on for peptic ulcer the incidence of carcinoma of the stomach is greatly increased. There is a very close relationship between the development of cancer and the presence of atrophic gastritis and intestinal metaplasia (Morson, 1955a; Siurala and Seppäla, 1960; Blackburn et al., 1968). It is equally well known that ulcers in different parts of the stomach are associated with a different distribution of gastritis and that gastritis progresses after the ulcer has been treated (Gear et al., 1971). Thus it is important to know how the extent of atrophic gastritis and intestinal metaplasia associated with gastric ulcers in different sites compares with that associated with carcinoma of the stomach and how previous surgery may alter the situation. We have therefore examined gastrectomy specimens from patients operated on for carcinoma and gastric ulcer and paid particular attention to the type and distribution of chronic gastritis and the presence of intestinal metaplasia, the site of the ulcer or cancer and any previous surgery.

Materials and methods

Stomachs from all gastrectomies performed in the Radcliffe Infirmary, Oxford, from 1970 to 1973 were examined. Gastrectomy specimens prior to 1970 were deemed unsuitable because the sampling was limited and not accurately recorded. Consequently, a prospective study was planned and the stomachs were opened along the greater curve, just anterior to the omentum, and pinned out on to a cork board before being placed into standard 10 per cent formol–saline fixative for 2 days. The position of the ulcer or tumour was noted.

Following fixation, blocks of tissue between 2·5 and 3·5 cm in length were taken as follows:

1. Along the entire lesser curve.
2. Alternate blocks along the greater curve but always including the lines of resection.
3. Two blocks from the posterior wall and two from the anterior wall of the body area of the stomach.
4. Through the ulcer or cancer if not already included in blocks 1–3.

Sections 4–5 μ in thickness were cut and stained by haemotoxylin and eosin, periodic acid-Schiff, Foot's reticulin and a modified Maxwell's method (*see* Whitehead, 1973). One case of sarcoma and one of secondary malignant melanoma were excluded. In each block the presence of superficial gastritis, atrophic gastritis and intestinal metaplasia was noted, as defined in the classification of gastritis of Whitehead (1973). No attempt was made to grade the lesions.

For the purposes of this study the pyloric region is defined as that area of stomach in the fixed specimens bounded at its lower end by the duodenal mucosa and at its upper end by a line drawn between a point 2 cm above the duodenal mucosa on the greater curve and 4 cm on the lesser curve. The pyloric region does of course vary in extent, and pseudopyloric metaplasia is often present on the lesser curve near the margins of ulcers even when they are very high. Our definition consequently is one of convenience, in order to record the information. Ulcers occurring in this zone were termed 'pyloric ulcers' and in the rest of the stomach 'body ulcers'.

Results

The results are shown in *Table I.* Atrophic gastritis and intestinal metaplasia are uncommon in pyloric ulcers and occur almost entirely in the pyloric region as defined, or in the adjacent lesser or greater curve blocks. The less severe lesion of superficial gastritis alone is also seen in the pyloric region in about half the pyloric ulcer cases. In body ulcers the distribution is more widespread and in nearly all cases was seen in all the blocks. This distribution is similar to that seen in cases of cancer.

In the cases of gastrectomy following previous gastrojejunostomy for duodenal ulcer (in 3 cases associated with stomal ulcer and 3 with pyloric ulcer) the distribution of atrophic gastritis and intestinal metaplasia is again similar to that in cancer.

Discussion

Although Stalsberg and Taksdal (1971) found that there was no correlation between the extent of gastritis and metaplasia in gastrectomy specimens

---

* Department of Pathology, Radcliffe Infirmary, Oxford. Requests for reprints to R. Whitehead.

Table I: DISTRIBUTION OF ATROPHIC GASTRITIS, INTESTINAL METAPLASIA AND SUPERFICIAL GASTRITIS

Ulcer type	No. of cases	Atrophic gastritis						Intestinal metaplasia						Superficial gastritis					
		P	LC	LGC	UGC	BA	BP	P	LC	LGC	UGC	BA	BP	P	LC	LGC	UGC	BA	BP
Body	23	23	23	20	19	19	21	21	21	18	18	19	21	0	0	0	2	1	0
Pyloric	14	5	4	3	2	0	0	3	3	3	2	0	0	8	1	1	0	0	0
After gastrojejunostomy																			
Pyloric	3	3	3	3	3	2	1	3	3	3	3	2	1	0	0	0	0	1	0
Stomal	3	3	3	3	3	3	3	3	3	3	2	3	2	0	0	0	0	0	0
Cancer	21	19	19	19	20	20	18	19	19	18	18	18	17	0	0	0	0	0	0

P = pyloric region; LC = lesser curve above the pyloric region; LGC = lower greater curve; UGC = upper greater curve; BA = anterior wall body mucosa; BP = posterior wall body mucosa.

when operation was carried out for a benign condition and whether or not the patient subsequently developed cancer, they employed rather limited sampling of the specimens and did not clearly indicate the type of lesion for which the gastrectomy was carried out.

Our findings for gastritis and metaplasia in gastric ulcer and cancer are similar to those made by Magnus (1946) and Morson (1955b), but neither of these authors distinguished between pyloric and body ulcers.

Our findings also confirm those made by Gear et al. (1971) in a multiple fibre-optic biopsy study. The gastritis is widespread in association with ulcer of the body of the stomach and more localized distally in the stomach with prepyloric ulcer. Gear et al. (1971) found less intestinal metaplasia, but this is explained by the fact that it is often a patchy lesion and the bigger the sample of tissue the more likely it is to be found.

The distribution of atrophic gastritis and intestinal metaplasia associated with duodenal ulcer (Morson, 1955a) is identical to the distribution we have shown in prepyloric ulcer. This is perhaps not surprising since clinically they behave in a similar manner (Johnson, 1957). We have not been able to examine ordinary gastrectomy specimens in duodenal ulcer but we have confirmed the presence and distribution of gastritis in a fibre-optic biopsy study (Whitehead, 1974). It is of some importance that in 6 cases of duodenal ulcer treated by gastrojejunostomy and subsequent gastrectomy for recurrent ulcers (stomal 3 and pyloric 3) the stomach had a pattern of gastritis comparable to that seen in body ulcer. This distribution is the same as that seen in cancer of the stomach. It has been designated type B gastritis (Strickland and Mackay, 1973) to distinguish it from type A, i.e. that which is associated with pernicious anaemia. There is considerable evidence that type B gastritis precedes carcinoma (Siurala and Seppälä, 1960; Siurala et al., 1966; Imai et al., 1971; Walker et al., 1971). There is every indication, therefore, that patients with gastric ulcer in the body are more cancer-prone than those with ulcer in the pylorus or duodenum.

Whilst surgery in the treatment of peptic ulcer obviously has an established place it would appear that there is room for the investigation of methods of treatment of duodenal and pyloric ulcers which would obviate the change into 'cancer' pattern gastritis after operation. Gastro-enterostomy operations seem to be particularly prone to cause widespread atrophic gastritis and intestinal metaplasia (Kobayashi et al., 1970) and our findings support this. Operations which conserve the anatomy of the stomach, e.g. highly selective vagotomy, may prove to have a less deleterious effect in terms of subsequent gastritis. As far as body ulcers are concerned, there is a case in ideal circumstances for careful periodic follow-up by endoscopy and biopsy following operation.

Acknowledgements

Dr Whitehead is in receipt of a grant reference BECC/1, CC/281 from the British Empire Cancer Campaign for Research for technical assistance. The authors would like to thank Mrs Rachel Hunt for typing the manuscript.

References

BLACKBURN E. K., CALLENDAR S. T., DACIE J. V., DOLL R., GIRDWOOD R. H., MOLLIN D. L., SARACCI R., STAFFORD J. L., THOMPSON R. B., VARADI S. and WETHERLEY-MEIN G. (1968) Possible association between pernicious anaemia and leukaemia: a prospective study of 1625 patients with a note on the very high incidence of stomach cancer. *Int. J. Cancer* 3, 163–170.

GEAR M. W. L., TRUELOVE S. C. and WHITEHEAD R. (1971) Gastric ulcer and gastritis. *Gut* **12**, 639–645.

IMAI T., KUBO T. and WATANABE H. (1971) Chronic gastritis in Japanese with reference to high incidence of gastric carcinoma. *J. Natn. Cancer Inst.* **47**, 179–195.

JOHNSON H. D. (1957) Etiology and classification of gastric ulcers. *Gastroenterology* **33**, 121–123.

KOBAYASHI S., PROLLA J. C. and KIRSNER J. B. (1970) Late gastric carcinoma developing after surgery for benign conditions. Endoscopic and histologic studies of the anastomosis and diagnostic problems. *Am. J. Dig. Dis.* **15**, 905–912.

MAGNUS H. A. (1946) The pathology of simple gastritis. *J. Pathol. Bact.* **58**, 431–439.

MORSON B. C. (1955a) Carcinoma arising from areas of intestinal metaplasia in the gastric mucosa. *Br. J. Cancer* **9**, 377–385.

MORSON B. C. (1955b) Intestinal metaplasia of the gastric mucosa. *Br. J. Cancer* **9**, 365–376.

SIURALA M. and SEPPÄLA K. (1960) Atrophic gastritis as a possible precursor of gastric carcinoma and pernicious anaemia. Results of follow-up examinations. *Acta Med. Scand.* **166**, 455–474.

SIURALA M., VARIS K. and WILJASALO M. (1966) Studies of patients with atrophic gastritis: a 10–15 year follow-up. *Scand. J. Gastroenterol.* **1**, 40–48.

STALSBERG H. and TAKSDAL S. (1971) Stomach cancer following gastric surgery for benign conditions. *Lancet* **2**, 1175–1177.

STRICKLAND R. G. and MACKAY I. R. (1973) A reappraisal of the nature and significance of chronic atrophic gastritis. *Am. J. Dig. Dis.* **18**, 426–440.

WALKER I. R., STRICKLAND R. G. and UNGAR B. (1971) Simple atrophic gastritis and gastric carcinoma. *Gut* **12**, 906–911.

WHITEHEAD R. (1973) *Mucosal Biopsy of the Gastro-intestinal Tract.* London, Saunders, p. 2.

WHITEHEAD R. (1974) Unpublished observations.

Br. J. Surg. Vol. 62 (1975) 26–32

A clinicopathological review of 68 carcinomas of the gallbladder

L. A. DONALDSON AND A. BUSUTTIL*

SUMMARY

A clinical and pathological review of 68 patients with a primary carcinoma of the gallbladder was undertaken. A prolonged preceding history of biliary disease was noted. Preoperative radiological and biochemical investigations were not helpful, but an isolated elevation in serum alkaline phosphatase level in the absence of any biliary obstruction or hepatic dysfunction was noticed in some patients. The significance of stones in relation to pathogenesis is discussed. A more radical surgical approach involving a partial hepatectomy appears to be the only possible treatment in view of the mode of spread of this tumour and the bad overall prognosis.

IN general surgical practice the incidence of tumours of the gallbladder is often considered negligible, yet Chandler and Fletcher (1963) noted that it accounts for about one-fifth of all carcinomas of the gastrointestinal tract. Graham (1931) has shown that it represents 8–10 per cent of all malignant disease in women, and Arminski (1949) found it occurring in 4·5 per cent of all cancer autopsies; Cooke et al. (1953) believed it to account for about 1 per cent of all carcinomas in Britain. Ross and Hickok (1960) reported that 7 per cent of all surgically removed gallbladders in patients over 70 years of age contain a primary malignant growth, and Horwitz and Rosenweig (1960) suggested an incidence of 6 per cent in patients over 50 years. Despite its reported frequency, the diagnosis and treatment of tumours of this site are surrounded by an aura of utter despondency and hopelessness (Leading Article, 1971).

A study of this problem was undertaken by reviewing all the patients in whom such a diagnosis was established in the Western and Victoria Infirmaries in Glasgow between the years 1961 and 1973 inclusive. A total of 68 cases was collected from the routine histopathological and autopsy records; 4361 intact gallbladders and gallbladder biopsies were submitted for histological examination and the incidence of carcinoma in them was 1·2 per cent (53 cases). Over this same time interval 10 748 autopsies were carried out in which there were 27 histologically confirmed cases (namely 0·25 per cent of the total examinations). Twelve of our cases were diagnosed initially at laparotomy and subsequently came to autopsy examination. During this same period the incidence of gallstones in autopsy examinations was also recorded (*Table I*).

Table I: INCIDENCE OF GALLBLADDER CALCULI IN 10 748 AUTOPSIES

Age (yr)	Sex (% patients) Male	Female
<60	3·4	10
60–64	7	14
65–69	11	25
70–74	13	27
75–79	20	35
[illegible]80	22	35

Presenting symptoms and signs

On admission 51 of the patients had symptoms and signs of an acute on chronic cholecystitis; 18 were also jaundiced and 25 had a palpable right hypochondrial mass (*Table II*). Eight other patients presented with painless jaundice and the findings at clinical examination were unremarkable. Another 3 patients complained of vague generalized dull abdominal pain alone, but on examination a tender mass was palpable in 1 patient, and in another in whom upper abdominal tenderness was detectable the diagnosis was made at laparotomy. The remaining 6 cases were diagnosed solely at necropsy examination and biliary symptoms had not been recorded during life.

Table II: PRESENTING SYMPTOMS AND SIGNS IN 68 PATIENTS

Symptom	No. of cases	Right hypochondrial mass
Biliary dyspepsia	33	14
Biliary dyspepsia and jaundice	18	11
Painless jaundice	8	0
Generalized abdominal pain	3	1
No biliary symptoms, diagnosed at autopsy	6	0

In 1 of the latter patients death was due to disseminated malignancy, but in the other cases the carcinoma was an incidental finding and not a direct cause of death. The duration of gallbladder dysfunction exceeded 1 year in 25 patients (*Fig.* 1). This history was substantiated in 5 patients by the occurrence of a cholecystostomy with removal of calculi over 15 years previously, and in 9 other patients by a record of a nonfunctioning gallbladder observed during cholecystograms carried out during former hospital attendance many years previously. Concomitant maturity-onset diabetes mellitus was known to be present in 6 patients. Weight loss was not a prominent feature even in the advanced cases.

---

* University of Glasgow, Department of Pathology, Western Infirmary, Glasgow G11 6NT.
Correspondence and reprints to Dr A. Busuttil.

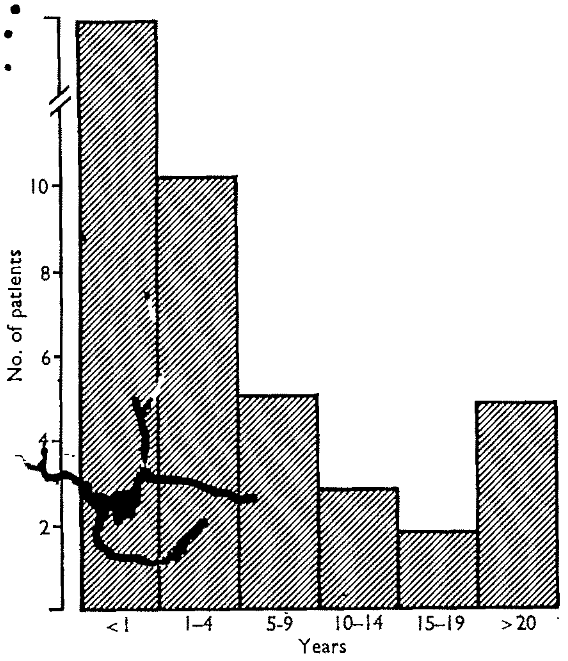


Fig. 1. Length of biliary dysfunction prior to final presentation.

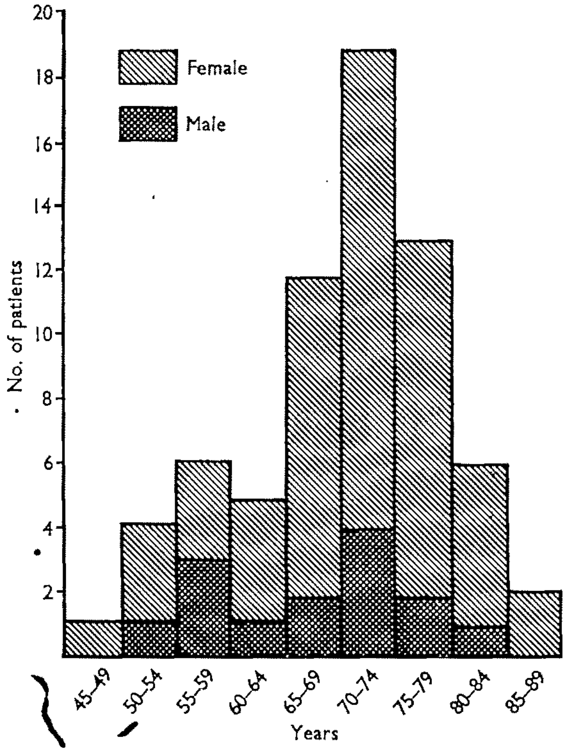


Fig. 2. Age and sex distribution.

The ratio of males to females in this series was 1 : 4 and the overall mean age of the male patients was 67 years and that for the females 71 years. The detailed distribution by age and sex is shown in *Fig.* 2.

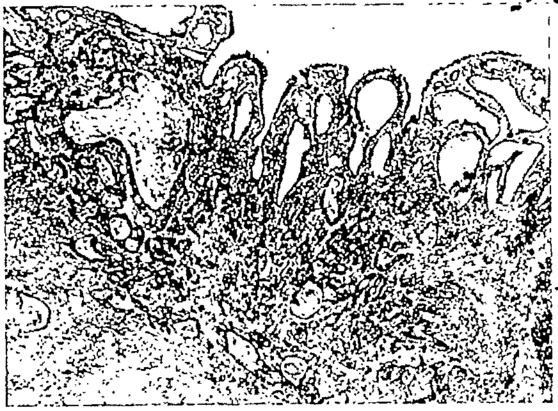


Fig. 3. Primary adenocarcinoma of the gallbladder. (× 175.)

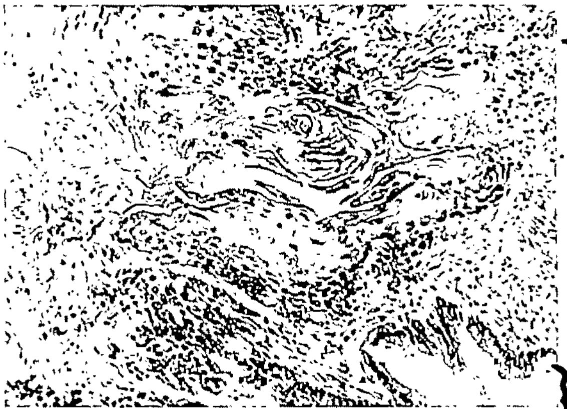


Fig. 4. Primary keratinizing squamous cell carcinoma of the gallbladder. (× 175.)

Thirty-seven patients underwent radiological investigation (*Table III*). In none of these cases was a carcinoma of the gallbladder diagnosed and in all the patients undergoing a cholecystogram a nonfunctioning gallbladder was found. In 2 of the 7 patients undergoing barium studies the findings suggested a gastric carcinoma.

Preoperative biochemical tests of hepatic function were available in 35 patients (*Table IV*). The only finding of note was an elevation of serum alkaline phosphatase in conjunction with a normal serum bilirubin and normal transaminases (aminotransferases) in 10 cases. In these patients there was no overt evidence of metabolic bone disease.

Fifty-three patients were subjected to a laparotomy and in 14 of them a cholecystectomy was performed (*Table V*). Although no clinical suspicion of malignancy was entertained, in 10 of the latter patients, on reviewing the surgeon's notes, the operative procedure was considered 'difficult' as multiple adhesions bound down the gallbladder to the liver. In the other 4 cases the suspicion of malignancy was raised at the actual time of the operation and subsequently confirmed histologically. In the remaining 39 patients dissemination of the carcinoma prevented any definitive or palliative procedures, although 6 of the

Table III: RADIOLOGICAL FINDINGS IN 37 CASES

Radiology	No. of cases	
Straight X-ray of the abdomen		9
Gallstones visualized	7	
Normal	2	
Oral then intravenous cholangiogram		27
Non-functioning gallbladder	24	
Non-functioning with stones	3	
Normal	0	
Suggesting carcinoma	0	
Barium meal examination		7
Normal	5	
Extrinsic duodenal deformity	2	

Table IV: LIVER FUNCTION TESTS IN 35 CASES

Test	No. of cases
Normal bilirubin Normal transaminases Normal SAP	9
Normal bilirubin Normal transaminases Elevated SAP	10
Elevated bilirubin Normal transaminases Normal SAP	2
All elevated	14

SAP, Serum alkaline phosphatase.

patients who had an empyema of the gallbladder underwent a drainage procedure. Three of the gallbladders removed surgically also showed an empyema.

Table V: TIME OF DIAGNOSIS

Diagnosis	No. of cases
Diagnosed as inoperable at laparotomy and biopsied	39
Diagnosed in surgically removed gallbladders	
a. Not clinically suspected	10
b. Clinically suspicious	4
Diagnosed at autopsy	
a. Unsuspected clinically in the presence of biliary symptoms	9
b. Unsuspected clinically in the absence of biliary symptoms	6

Table VI: STAGING BY EXTENT OF SPREAD AT LAPAROTOMY

Extent of spread	Total no. of cases	Survival (mth)				
		1	3	6	>6	N/A
Localized to gallbladder	12	2	2	—	6	2
Spread solely to local lymph nodes	10	5	3	2	—	—
Minimal liver involvement in gallbladder bed alone	6	3	1	[illegible]	—	2
Spread to local lymph nodes and minimally to right liver lobe beyond gallbladder bed	11	9	—	2	—	—
Massive spread to right liver lobe ± lymph nodes	10	6	2	—	—	2
Generalized peritoneal dissemination	3	2	1	—	—	—
Direct invasion of colon	1	1	—	—	—	—
Total	53	28	9	4	6	6

Three patients survived for longer than 3 years; the longest survival was 8 years.
N/A, No information available.

Pathology

Histological examination showed that 74 per cent of all the tumours were adenocarcinomas of varying differentiation; squamous cell carcinoma and anaplastic carcinoma accounted for 4·4 and 11·6 per cent respectively (*Figs.* 3, 4). In one autopsy a primary spindle cell sarcoma was discovered. In the remaining 6 cases the histological type was not specified.

Gallstones were present in addition to the tumour in 47 cases (70 per cent). Forty-five had multiple faceted stones and the other 2 were cholesterol in type. No information was available for the other 9 cases.

In order to assess the prognosis in the cases that underwent surgery, staging was attempted according to the extent of spread of the tumour (*Table VI*). In 22 cases the carcinoma either was limited solely to the gallbladder (12 cases) or had spread to involve the cystic lymph node and the other nodes in the immediate vicinity of the cystic and common bile ducts (10 cases). Spread to the right lobe of the liver had already occurred in the remaining cases. However, in 17 of these patients the spread was limited to the gallbladder bed with minimal superficial infiltration of hepatic parenchyma. Local spread to the colon had occurred in 1 case and in 3 other cases there was generalized peritoneal spread. The pattern of spread in the autopsy cases confirmed the impression at operation: this tumour spreads mainly by local infiltration into the right lobe of the liver and through the lymphatics to the nodes along the common bile duct. Vascular dissemination to the lungs (6 cases), lumbar spine (2 cases) and heart (1 case) was also recorded.

In none of the patients were any radical operative procedures attempted and the only survivors for longer than 6 months were those in whom the tumour was an incidental histological finding in a cholecystectomy specimen.

Discussion

There have been many reviews in the American literature of carcinoma of the gallbladder (Arminski, 1949; Gerst, 1961; Chandler and Fletcher, 1963; Holmes and Mark, 1971; Keill and De Weese, 1973), but very few have been documented in Great Britain (Illingworth, 1935; Solan and Jackson, 1971).

In the 57 cases collected by Solan and Jackson (1971) the female to male ratio was 2·6 : 1; likewise in the Swedish series of 58 cases documented by Hafström et al. (1973). In the 132 cases of Gerst (1961) the ratio was 3 : 1, and this also was shown in the cumulative review of 1061 cases for the years 1948–58 undertaken by Strauch (1960). These results concur with the fourfold higher incidence of this tumour in females noted in the present series.

There has been no significant variation of the age distribution between the sexes in this and other series (Solan and Jackson, 1971; Hafström et al., 1973), although it tends to present about 5 years earlier in male patients. This finding differs marginally from the experiences of Bossart et al. (1962), who in a survey of 76 cases found the disease occurring 10 years earlier in females.

Usually this tumour is discovered unsuspectedly at a laparotomy with a view to biliary surgery and in most series there is a low incidence of preoperative diagnosis. In the cumulative review of Strauch (1960) there were 482 gallbladder carcinomas in 34 242 biliary tract operations, representing an incidence of 1·4 per cent; Marcial-Rojas and Medina (1961) found this malignancy in 1·3 per cent of 2813 surgically removed gallbladders. In contrast, Holmes and Mark (1971) encountered 22 carcinomas of the gallbladder during 1816 cholecystectomies, an incidence of 1·21 per cent. In addition, in a further 38 patients undergoing a cholecystostomy 22 additional primary carcinomas were diagnosed, giving an incidence of 2·35 per cent in 1854 operations on the biliary tree. Keill and De Weese (1973) treated 33 patients with a primary gallbladder malignancy between 1957 and 1971 and during that time 1404 cholecystectomies were also performed; their stated incidence of 2·35 per cent is unusually elevated, but only 13 of their patients were actually submitted to a cholecystectomy.

Carcinoma was present in 0·32 per cent of the surgically removed gallbladders in this series. Bossart et al. (1962) found an incidence of 0·82 per cent; similarly Magee and MacDuffee (1968) and Seltzer et al. (1970) found the occurrence of carcinoma to be 1·1 and 0·6 per cent respectively, when each reviewed over 1000 cholecystectomies in an assessment of the postoperative mortality and morbidity. Thus it is apparent that an accurate estimate of the true incidence of this tumour proves very difficult, but it seems to be lower in Britain.

In this review the incidence of carcinoma of the gallbladder found at autopsy was 0·25 per cent. This is similar to the finding of Illingworth (1935) of 0·42 per cent, of Arminski (1949) of 0·43 per cent and of Marcial-Rojas and Medina (1961) of 0·18 per cent.

Although in most cases at autopsy or laparotomy the tumour can be confidently localized to the gallbladder as the site of origin, in a proportion of surgical cases the spread is already so extensive that only guarded speculation as to a possible origin within the biliary tract is possible. Even after a detailed dissection at autopsy the site of origin may still be difficult to determine, as multifocal carcinomas affecting the walls of the gallbladder and bile ducts simultaneously are on record (Willis, 1942).

A striking feature of the current series is the occurrence of longstanding biliary disease, which was proved in 33 patients radiologically and/or surgically; in some cases this was recorded several years prior to the final admission and diagnosis of the carcinoma (*Fig.* 1). Twenty-five (50 per cent) of our patients complained of biliary symptoms for longer than 1 year and 15 patients had symptoms exceeding 4 years. A shorter duration of biliary history was noted by Holmes and Mark (1971), who found that in only 28 per cent of their patients had there been symptoms for longer than a year. Thirty-nine per cent of the patients reviewed by Keill and De Weese (1973) had symptoms for longer than 2 years, and half of the cases reviewed by Marcial-Rojas and Medina (1961) had such complaints for between 6 months and 10 years. There was a very variable duration of biliary history in the cumulative review by Strauch (1960). Two-thirds of the 22 patients studied by McLaughlin (1964) and half of the patients reviewed by Glenn and Hays (1954) had biliary symptoms lasting for longer than 1 year. Both Illingworth (1935) (50 cases) and Horwitz and Rosenweig (1960) (20 cases) remarked about the very prolonged antecedent biliary history in some of their patients. However, Solan and Jackson (1971) found that only 13 per cent of their patients gave any previous history of biliary disease. These wide variations in the duration of preceding biliary symptoms may be due in part to the failure of recall by the patient; a number of patients in our series failed to recollect any previous biliary trouble in spite of having undergone a cholecystostomy or a cholecystogram in the past.

Robertson and Carlisle (1967) and Holmes and Mark (1971) noted that the most frequent symptom complex was indistinguishable from 'benign' biliary disease. In contrast, Strauch (1960) considered that most patients could pinpoint the transformation of a 'benign' to a 'malignant' lesion to within a week of its occurrence; Horwitz and Rosenweig (1960) remarked that a change in the pattern of pain was frequently the reason why their patients sought medical attention, the character of the pain changing to a persisting, severe, unremitting type. This feature was not confirmed in other series (Marcial-Rojas and Medina, 1961; Keill and De Weese, 1973) or in this series.

The typical cachectic and emaciated picture of a malignancy was not part of our clinical experience and even the tumours that had disseminated widely via the bloodstream failed to produce significant weight loss. Obesity prior to the development of the tumour may account for this finding and most of our patients coming to autopsy were obese.

The unhelpful (or misleading) radiological findings noted (*Table III*) are essentially similar to those of Chandler and Fletcher (1963), Solan and Jackson (1971) and Keill and De Weese (1973). Thirty-seven of our patients underwent radiological investigation of the abdomen, and calcified biliary calculi were noted in 8 cases. This is a marginally high incidence (21 per cent) when compared with the findings of Sherlock (1968), who stated that only 10 per cent of gallstones are radio-opaque. In 22 per cent of totally calcified gallbladders—the so-called 'porcelain gallbladder'—a malignancy was revealed (Polk, 1966); in the only case of this type seen at the Western Infirmary during the past 10 years there was no evidence of malignancy (Busuttil and McLean, 1974). Dystrophic calcification of the gallbladder wall is probably an indication of the duration of the biliary dysfunction, and this adds weight to the argument that prolonged biliary dysfunction may predispose to carcinomatous change (Cornell and Clarke, 1959).

The deposition of sufficient calcium salts within gallstones as to make them radio-opaque may have a similar significance.

Of the biochemical investigations of liver function available in 35 cases (*Table IV*), the serum alkaline phosphatase (SAP) estimation was the most rewarding. As expected, in cases with partial or complete extrahepatic occlusion of the common bile duct the level of the SAP invariably exceeded 30 King-Armstrong (KA) units/100 ml. However, it was also noted that in 10 cases (28 per cent of the patients with known liver function tests) there was an elevated SAP (in 1 case to 65 KA/100 ml) without any evidence of biliary obstruction at that time. Solan and Jackson (1971) also noted this finding in 8 of their 10 anicteric patients, and Hafström et al. (1973) in 8 of their 48 cases biochemically investigated. Other series have commented on the elevated SAP (Chandler and Fletcher, 1963; Hardy and Volk, 1970), but do not give any indication as to the proportion of the patients in which this was an isolated biochemical abnormality. Although these figures are small, there is a suggestion that an isolated elevation of the SAP taken in conjunction with a history of prolonged biliary dyspepsia might acquire a sinister significance. Sherlock (1968) has shown that this is a feature of early intrahepatic cholestasis; in all of our 10 patients with isolated SAP elevations there was involvement of the hepatic gallbladder bed to a variable degree.

The manner in which the 68 tumours in this series disseminated confirms previously documented experiences (Cooper, 1937; Arminksi, 1949; Fahim et al., 1962; Hafström et al., 1973). The tumour spreads locally and by lymphatics much earlier than by the bloodstream. Fahim et al. (1962), in a detailed discussion of the lymphatic drainage of the gallbladder, have shown that its lymphatic channels lead to the cystic lymph node and from there to the pericholedochal nodes on the right side of the common bile duct which in turn drain into the pancreatoduodenal and para-aortic nodes. The lymph nodes in the porta hepatis along the hepatic artery do not drain the gallbladder but only the left lobe of the liver. The nodes along the common bile duct are capable of a degree of enlargement sufficient to cause obstructive jaundice, while the liver and the more distal lymphatics are spared completely. An erroneous impression of unresectability at laparotomy was proved to be incorrect at autopsy in some of our early postoperative deaths.

Usually the presence of hepatic metastasis in a patient with an intra-abdominal tumour is considered to be a sign of advanced malignancy as such spread is assumed to be haematogenous in nature. However, the close proximity of the gallbladder to the hepatic parenchyma lends itself to relatively early direct spread to the liver without vascular involvement having occurred. The liver bed possibly becomes involved at an even earlier stage than the lymph nodes (Hafström et al., 1973). Seventeen of our cases coming to autopsy showed that the liver was involved only in the immediate vicinity of the gallbladder; more distal portions of the liver and the lymphatics were spared.

In view of this preferential mode of spread and the poor outlook in untreated cases (Strauch, 1960; Solan and Jackson, 1971) the prospects of a partial hepatic resection as part of a more radical approach to the tumour are worth consideration. Advances in surgical techniques, liver anatomy and pre- and postoperative hepatic pathophysiology have made such elective major hepatic resections for primary and metastatic tumour entirely possible (Foster, 1970). However, Glenn and Hays (1954) considered that only 20 per cent of their patients were suitable for their 'radical cholecystectomy' involving a resection of the gallbladder's liver bed, the peritoneum and retroperitoneal tissues of the gastrohepatic and pericholedochal areas. Fahim et al. (1962) observed that of their 20 patients who had undergone cholecystectomy and liver resection, 18 were dead within 18 months with only 1 patient surviving for 5 years; Brasfield (1961) reported a single case who was alive and well 5 years after having undergone similar surgery. Although Fahim et al. (1963) have stated that on anatomical and pathological grounds the treatment of early stage gallbladder carcinoma should be a cholecystectomy with wedge resection of the liver and a local nodal dissection, and in more advanced cases a right hepatic lobectomy, these procedures have been adopted only very infrequently. In Foster's (1970) review of 14 cases, though no prolonged survival was observed, there was absence of any residual tumour months and years postoperatively.

Recurrent cholecystitis and gallstones have been inculpated over the years with a causative role in primary gallbladder carcinoma (Arminski, 1949; Strauch, 1960; Marcial-Rojas and Medina, 1961; Holmes and Mark, 1971). In positive support of this, carcinomatous change of the gallbladder's epithelium has been induced through the introduction of methylcholanthrene pellets into the gallbladder of experimental animals (Fortner, 1955; Fortner and LeHall, 1961). However, in a review of this experimental evidence by Willis (1967) the production of such tumours seems to be species-specific and not easily reproducible. Burrows's (1933) review of the earlier experimental work also showed that although a 'polypoidal cholecystitis' had been produced no clearly malignant lesions were encountered. Furthermore, it is generally agreed that gallbladders exhibiting a primary malignancy almost invariably contain calculi as well. However, a third of the patients reviewed by Arminski (1949) and Strauch (1960) did not have concomitant cholelithiasis.

Gallstones are not uncommon incidental findings at necropsy, and in our own autopsy series (*Table I*) the overall incidence was 14 per cent and the occurrence in patients over 60 years of age was 18 per cent. Similarly, Cleland (1953) found an overall incidence of 8 per cent in 7000 consecutive autopsies, and Marcial-Rojas and Medina (1961) an incidence of 10·2 per cent in 1100 autopsies. The association of carcinoma with cholelithiasis also may be purely accidental.

Arminski (1949) postulated an irritative role for calculi which over the years resulted in recurrent ulcerative inflammation, reparative proliferation and regenerative hyperplasia with the eventual supervention of neoplasia, but mucosal hyperplasia and dysplasia are rare histopathological features in cholelithiasis. In the present series 7 per cent of the cases produced an antecedent history of cholecystostomy which suggested longstanding biliary tract infection and dysfunction; this was also noted in some of the series reviewed by Arminski (1949) and sporadically in other series (Keill and De Weese, 1973). However, Lund's (1960) long term follow-up of 526 patients with abnormal cholecystograms and that of Wenckert and Robertson (1966) of 781 similar patients revealed only 8 primary carcinomas of the gallbladder and these were in patients with non-functioning gallbladders.

In most series about 3 per cent of all primary carcinomas of the gallbladder are squamous in type which suggests an origin from metaplastic epithelial foci. This tumour is also commoner in females, who also have a higher incidence of calculi. Gallstones predispose to recurrent bacterial cholecystitis often due to coliform organisms, the incidence of positive culture of bile increasing with the age of the patient (Pyrtek and Bartus, 1967; Mason, 1968). Within the large intestine, coliform organisms have been shown capable of degradation of bile salts to carcinogenic agents (Aries et al., 1969); these organisms may possibly play a similar role within the gallbladder.

Acknowledgements

We gratefully acknowledge the co-operation of our surgical colleagues at the Western Infirmary and the Victoria Infirmary, Glasgow, and that of Dr J. Craik, Consultant Pathologist, Victoria Infirmary. We thank Professor J. R. Anderson and Dr R. N. MacSween for their criticism and help with this review.

References

ARIES V., CROWTHER J. S., DRASAR B. D., HILL J. R. J. and WILLIAMS R. E. O. (1969) Degradation of bile salts by human intestinal bacteria. *Gut*, **10**, 334–335.

ARMINSKI T. C. (1949) Primary carcinoma of the gallbladder. *Cancer* **2**, 379–398.

BOSSART P. A., PATTERSON A. H. and ZINTEL H. A. (1962) Carcinoma of the gallbladder. A report of seventy-six cases. *Am. J. Surg.* **103**, 366–369.

BRASFIELD R. D. (1961) Right hepatic lobectomy for carcinoma of the gallbladder: a five year cure. *Ann. Surg.* **153**, 563–566.

BURROWS H. (1933) Experimental inquiry into association between gallstones and primary cancer of gallbladder. *Br. J. Surg.* **20**, 607–629.

BUSUTTIL A. and MCLEAN N. (1974) A porcelain gallbladder. *Br. J. Clin. Pract.* In the press.

CHANDLER J. J. and FLETCHER W. S. (1963) A clinical study of primary carcinoma of the gallbladder. *Surg. Gynecol. Obstet.* **117**, 297–300.

CLELAND J. B. (1953) Gall-stones in 7000 post mortem examinations. *Med. J. Aust.* **26**, 488–489.

COOKE L., AVERY-JONES F. and KEICH M. K. (1953) Carcinoma of the gallbladder. A statistical study. *Lancet* **2**, 585–587.

COOPER W. A. (1937) Carcinoma of the gallbladder. *Arch. Surg.* **35**, 431–448.

CORNELL C. M. and CLARKE R. (1959) Vicarious calcification involving the gall-bladder. *Ann. Surg.* **149**, 267–272.

FAHIM R. B., FERRIS D. O. and MCDONALD J. R. (1963) Carcinoma of the gallbladder. An appraisal of its surgical treatment. *Arch. Surg.* **86**, 334–341.

FAHIM R. B., MCDONALD J. R., RICHARD J. C. and FERRIS D. O. (1962) Carcinoma of the gallbladder—a study of its modes of spread. *Ann. Surg.* **156**, 114–124.

FORTNER J. G. (1955) Experimental induction of primary carcinoma of gallbladder. *Cancer* **8**, 689–700.

FORTNER J. G. and LEHALL L. D. (1961) Carcinoma of the gallbladder in dogs. *Cancer* **14**, 1127–1130.

FOSTER J. H. (1970) Survival after liver resection for cancer. *Cancer* **26**, 493–502.

GERST P. H. (1961) Primary carcinoma of the gallbladder. A thirty year summary. *Ann. Surg.* **153**, 369–372.

GLENN F. and HAYS D. M. (1954) The scope of radical surgery in treatment of malignant tumours of the extrahepatic biliary tract. *Surg. Gynecol. Obstet.* **99**, 529–541.

GRAHAM E. A. (1931) Prevention of carcinoma of the gallbladder. *Ann. Surg.* **93**, 317–322.

HAFSTRÖM L., ZETTERGREN L. and ÅKESSON L. A. (1973) The natural history of primary and secondary malignant tumours of the liver. *Acta Chir. Scand.* **139**, 264–269.

HARDY M. A. and VOLK H. (1970) Primary carcinoma of the gallbladder. A ten year review. *Am. J. Surg.* **120**, 800–803.

HOLMES S. L. and MARK J. B. D. (1971) Carcinoma of the gallbladder. *Surg. Gynecol. Obstet.* **133**, 561–564.

HORWITZ A. and ROSENWEIG J. (1960) Carcinoma of the gallbladder—a real hazard. A summary of twenty cases. *JAMA* **173**, 234–236.

ILLINGWORTH C. F. W. (1935) Carcinoma of the gallbladder. *Br. J. Surg.* **23**, 4–18.

KEILL R. H. and DE WEESE M. S. (1973) Primary carcinoma of the gallbladder. *Am. J. Surg.* **125**, 726–729.

LEADING ARTICLE (1971) *Lancet* **2**, 967.

LUND J. (1960) Surgical indications in cholelithiasis: prophylactic cholecystectomy elucidated on the basis of long term follow-up on 526 non-operated cases. *Ann. Surg.* **151**, 153–162.

MCLAUGHLIN, C. W. (1964) Carcinoma of the gallbladder, an added hazard in untreated calculous cholecystitis in older patients. *Surgery* **56**, 755–759.

MAGEE R. B. and MACDUFFEE R. C. (1968) One thousand consecutive cholecystectomies. *Arch. Surg.* **96**, 858–862.

MARCIAL-ROJAS R. A. and MEDINA R. (1961) Unsuspected carcinoma of gallbladder in acute and chronic cholecystitis. *Ann. Surg.* **153**, 289–298.

MASON R. G. (1968) Bacteriology and antibiotic selection in biliary tract surgery. *Arch. Surg.* **97**, 533–537.

POLK H. C. (1966) Carcinoma and the calcified gallbladder. *Gastroenterology* **50**, 582–585.

PYRTEK L. J. and BARTUS S. A. (1967) Evaluation of antibiotics in biliary tract surgery. *Surg. Gynecol. Obstet.* **125**, 101–105.

ROBERTSON W. A. and CARLISLE B. B. (1967) Primary carcinoma of the gallbladder. Review of fifty-two cases. *Am. J. Surg.* **113**, 738–742.

ROSS F. P. and HICKOK D. F. (1960) Hernia and gallbladder surgery in patients over seventy. *New Engl. J. Med.* **262**, 501–505.

SELTZER M. H., STEIGER E. and ROSATO F. E. (1970) Mortality following cholecystectomy. *Surg. Gynecol. Obstet.* **130**, 64–66.

SHERLOCK S. (1968) *Diseases of the Liver and Biliary System*, 4th ed., ch. 28. Oxford, Blackwell.

SOLAN M. J. and JACKSON B. T. (1971) Carcinoma of the gallbladder—a clinical appraisal and review of 57 cases. *Br. J. Surg.* **58**, 593–597.

STRAUCH G. O. (1960) Primary carcinoma of the gallbladder. *Surgery* **47**, 368–383.

WENCKERT A. and ROBERTSON B. (1966) The natural course of gallstone disease: eleven year review of 781 non-operated cases. *Gastroenterology* **50**, 376–381.

WILLIS R. A. (1942) Some aspects of the pathology of carcinomata of biliary tract. *Med. J. Aust.* **2**, 340–344.

WILLIS R. A. (1967) *Pathology of Tumours*, 4th ed., ch. 25. London, Butterworths.

Br. J. Surg. Vol. 62 (1975) 33–36

Primary carcinoma of the gallbladder

A. T. M. PRAKASH, LALIT K. SHARMA AND P. N. PANDIT*

SUMMARY.
The clinical and pathological features of 100 consecutive cases of primary carcinoma of the gallbladder, treated by a single surgical unit, are described. Females outnumbered males by 2 to 1. The maximum incidence was seen in the fifth decade. Pain and the presence of a mass were the two most common clinical features. Gallstones coexisted in 45 per cent of cases. Ancillary investigations were of little value in preoperative diagnosis. At laparotomy biopsy alone was possible in a large number of cases owing to the advanced disease process. Two patients were alive 5 years after surgery. Prophylactic cholecystectomy for all diseased gallbladders, whether symptomatic or not, is advocated.

EVER since the first review of 100 cases of carcinoma of the gallbladder by Musser (1889), there has been little change in the outlook and survival rate of patients with this disease. The signs and symptoms of a resectable carcinoma of the gallbladder are similar to those of chronic cholecystitis and cholelithiasis. Persistent right upper quadrant pain, a hard gallbladder lump, jaundice and weight loss often suggest the diagnosis, but by then the disease is invariably inoperable. A 5-year survival is rare, unless an early lesion is found coincidentally in a gallbladder removed for chronic cholecystitis and cholelithiasis.

There are very few reports in the literature of a series of 100 or more cases of carcinoma of the gallbladder treated by a single team and particularly from India. The present article gives the experience of 100 cases of histologically proved carcinoma of the gallbladder, treated in the Professorial Unit of the All India Institute of Medical Sciences Hospital, New Delhi, over a period of 15 years from 1959.

Age and sex incidence

There were 68 females and 32 males, giving a female to male ratio of 2 : 1. The ages of the patients ranged from 30 to 75 years, the average being 49 years; the majority of patients, however, were between 40 and 50 years (*Fig.* 1).

Clinical features

A history suggestive of chronic cholecystitis of long duration was available in only 12 cases. Surprisingly, the average duration of symptoms in most patients was only 8 weeks.

Ninety-five patients complained of pain, often severe, usually in the epigastrium or right hypochondrium (*Fig.* 2). In the majority, it was a continuous ache. Less than 10 per cent of cases had colicky pain, with or without radiation. Seventy-five patients had marked anorexia and 70 of them had a significant weight loss. Nearly a quarter of the patients (24) complained of low grade fever. Seven patients presented with obstruction: 4 at the pylorus and 3 in the small bowel. None of these cases presented as acute cholecystitis.

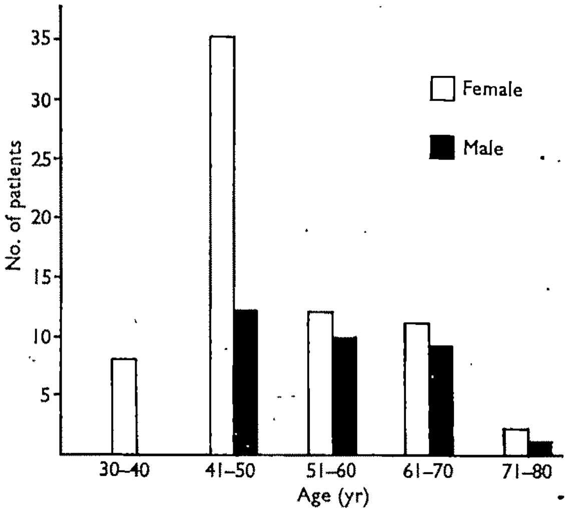


Fig. 1. Age and sex incidence.

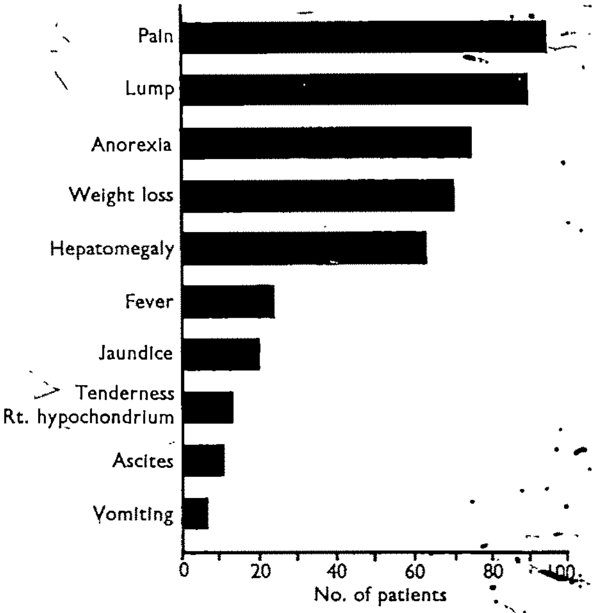


Fig. 2. Clinical features.

---

* Department of Surgery, All India Institute of Medical Sciences, New Delhi 110016, India.

In 92 cases there was a lump in the right hypochondrium which was often hard and irregular; 15 patients complained of pain over the lump. Hepatomegaly was present in 65 per cent and jaundice on admission was seen in 20 per cent of the patients. Ascites and tenderness under the right costal margin were less common.

Investigations

Radiology was of little help in diagnosis. Plain X-ray of the abdomen revealed radio-opaque calculi in only 8 cases. Oral cholecystography was carried out in 60 of the non-jaundiced patients, including 4 of those showing calculi on plain X-ray; in 2 patients only, was the gallbladder visualized faintly, and not at all in the remainder. A neoplastic filling defect in the gallbladder was never seen. In about half of the cases where an oral cholecystogram did not outline the gallbladder intravenous cholangiography was undertaken, but did not provide any additional information. Percutaneous transhepatic cholangiography was attempted in 10 of the 20 jaundiced patients; it failed in 2, the obstruction at the porta hepatis was seen in 6 and obstruction of the common hepatic duct in 2. These findings were confirmed at operation.

Routine chest X-ray revealed secondaries in the lungs in 2 cases. Barium meal, barium enema and intravenous pyelography were done when indicated. Barium meal examinations showed extrinsic pressure on the duodenum in 6 cases. Barium enema studies showed evidence of extrinsic pressure on the hepatic flexure on 3 occasions. Intravenous pyelography, done in 3 patients, did not contribute further information.

Biochemical investigations were of little assistance. The liver function tests were diagnostic of obstructive jaundice. However, in the absence of icterus, the serum alkaline phosphatase was elevated in about 25 per cent of the cases.

Association with gallstones

Gallstones were present in 45 patients. However, this may not represent the true number as in a majority of the inoperable cases a biopsy alone was done and the gallbladder was not opened.

Gross pathology (*Table I*)

The growth involved the gallbladder diffusely in 78 cases, it was in the fundus in 12 cases and the neck of the gallbladder was involved in 8 cases; Hartmann's pouch and the cystic duct were involved in 2 cases. In almost 75 per cent of the cases the tumour had infiltrated into the adjacent liver tissue.

Histology

Histologically, 90 per cent of the tumours were adenocarcinoma. Two were colloid carcinoma, 4 squamous cell carcinoma and 4 undifferentiated tumour.

Treatment (*Table II*)

Table I: GROSS PATHOLOGY

Site:	No. of cases:
Diffuse growth	78
Fundus	12
Neck	8
Hartmann's pouch	1
Cystic duct	1

Table II: OPERATIONS PERFORMED

Operation:	No. of cases:
Cholecystectomy	20
Cholecystectomy with wedge resection of liver	12
Cholecystectomy with resection of hepatic flexure	6
Biliary/intestinal short circuiting	10
Diagnostic laparotomy and biopsy	52

Cholecystectomy alone or with hepatic wedge resection was performed in 32 cases. Segmental resection of the hepatic flexure of the colon was an added procedure in 6 cases. Bypass procedures were done in 10 patients; 6 of these were for gastrointestinal obstruction and 4 for biliary obstruction. In the remainder the disease was too far advanced for any major surgical procedure; in these patients biopsy alone could be done from the gallbladder, liver, lymph nodes or omentum.

Survival

Twelve patients died within 1 month of the operation. Biliary peritonitis, hepatic coma and wound dehiscence were the main causes of death. Gastric dilatation was the cause of death in 1 patient. The cause of death was not known in 2 patients. Only 15 patients were alive 1 year after operation and 3 were alive after 3 years. The average survival time for the patients after operation was 6 months. Thus, the overall prognosis is gloomy. Two patients are alive 5 years after a 'curative' excision.

Discussion

The incidence of primary carcinoma of the gallbladder varies widely in different reports. In Britain less than 1 per cent of carcinomas arise in the gallbladder (Solan and Jackson, 1971). The condition appears to be more common in the United States (Holmes and Mark, 1971; Pemberton et al., 1971). In contrast, owing to the lack of a cancer registry, the actual incidence of carcinoma of gallbladder in India is subject to a variety of opinions. However, this series of 100 histologically proved cases over a period of 15 years from a single surgical unit indicates that the disease is not uncommon in India.

Almost all reports suggest that gallbladder carcinoma is predominantly a disease of middle-aged or elderly women. The female to male ratio of 2 : 1 in this series is typical. There are only one or two reports in the literature stating that the disease is more common in men (D'Aunoy et al., 1938), and these reports relate to small series.

The average age of 49 years in this series is lower than that mentioned in Western literature (Holmes and Mark, 1971; Solan and Jackson, 1971). Most of our patients were in the 40–50 age group. There was no sex difference in age incidence. The youngest patient in this series was a female aged 30 years. However, Rudolph and Cohen (1972) reported carcinoma of the gallbladder in an 11-year-old Navajo girl, this being the youngest patient reported so far.

The aetiology of carcinoma of gallbladder is not clear. Chronic infection, gallstones and benign neoplasms have been mentioned. The incidence of gallstones in association with carcinoma of the gallbladder varies from 54 to 100 per cent (Strauch and Providence, 1960; McLaughlin, 1964). Hart et al. (1971) stated that cholelithiasis plays a major part in the aetiology of gallbladder cancer. Comfort et al. (1948) could not find carcinoma of the gallbladder in 112 cases of asymptomatic biliary calculi followed over a period of 10–25 years. Warren and Blach (1940) reported that 2·5 per cent of patients of cholelithiasis would eventually develop carcinoma. In our series gallstones were present in 45 per cent of the cases. However, this may not represent the true figure, as in a large number of cases biopsy alone was obtained. A combination of factors such as chronic mechanical irritation, infection, local metabolic dysfunction, bile stasis and individual host susceptibility may play a role in the development of carcinoma of the gallbladder (Strauch and Providence, 1960; Solan and Jackson, 1971).

The clinical picture of carcinoma of the gallbladder is non-specific. A low clinical diagnosis rate is common in almost all reported series. This is accounted for by the indefinite symptoms and signs and the lack of help from ancillary investigations.

Gallbladder carcinoma is asymptomatic in its early and potentially curable stage. The clinical features in our patients were typical of late presentation. Pain in the epigastrium or right hypochondrium, anorexia, weight loss and low grade fever were the common symptoms. A right upper quadrant mass, hepatomegaly and jaundice were the most common physical signs. These clinical features have also been seen in the majority of cases reported in the literature. Solan and Jackson (1971) commented on the frequent history of long-standing biliary disease in association with gallbladder cancer, but this occurred in only 12 per cent of our cases.

Ancillary investigations are of little help in diagnosis. Anaemia, jaundice and disturbed liver functions are non-specific findings. Plain X-ray of the abdomen showed radio-opaque calculi in only 8 cases. Cholecystography, both oral and intravenous, usually showed a non-functioning gallbladder. A filling defect due to a neoplasm, as described by Samuel (1966), was never seen. Percutaneous transhepatic cholangiography can be a useful aid in jaundiced patients to decide the level and nature of the obstruction and to assess operability (Machado, 1971). Selective angiography has also been used by some workers, but its efficacy has yet to be established (Sato et al., 1969).

Adenocarcinoma is the commonest type of gallbladder carcinoma. This was confirmed in our series, followed by squamous cell, colloid and undifferentiated tumours. An almost similar incidence has been reported by other authors (Strauch and Providence, 1960). However, Litwin (1967) reported a higher number of undifferentiated carcinomas. The rare tumours like carcinoid, melanoma (Gradisar and Kelly, 1970) and angiosarcoma (Tanga and Ewing, 1970) were not seen in our series.

In the majority of our cases, only a diagnostic laparotomy and biopsy were possible. Several authors reported a similar experience (Litwin, 1967; Robertson and Carlisle, 1967; Solan and Jackson, 1971). Despite a fairly large number of curative excisions, only 2 patients lived for 5 years. One of them was operated upon for benign gallbladder disease and carcinoma was an incidental finding.

Uniformly bad prognosis has also been the experience of other workers. In the collective review published by Strauch and Providence (1960) the 5-year survival rate was 1 per cent out of a total of 1061 cases. No large series has reported a higher than 6 per cent 5-year survival rate.

The dismal outlook in gallbladder carcinoma is attributed mainly to three factors: elderly patients, early spread to the liver and lack of specific clinical features (Chandler and Fletcher, 1963). Fahim et al. (1962) described in detail the modes of spread of carcinoma of the gallbladder. Based on this and on our own experience, we tend to agree with Appleman et al. (1963) that radical surgery has a very limited role to play in improving the overall prognosis of gallbladder carcinoma.

Since early diagnosis is almost impossible and improvement of surgical technique has not altered the prognosis, the only way one can perhaps improve this dismal outlook is to emphasize prophylaxis.

Prophylactic cholecystectomy in cases of asymptomatic gallstones has been suggested on the grounds that it may prevent future cancer (Nield, 1964; Hart et al., 1971; Holmes and Mark, 1971). There are others who disagree with this contention (Solan and Jackson, 1971). Although there is no convincing proof that gallstones are carcinogenic, we feel that early cholecystectomy should be done for all cases of cholelithiasis, whether symptomatic or asymptomatic, provided that there is no surgical contraindication.

References

APPLEMAN R. M., MORLOCK C. G., DAHLIN D. C. and ADSON M. A. (1963) Longterm survival in carcinoma of the gallbladder. *Surg. Gynecol. Obstet.* **117**, 459–464.

CHANDLER J. J. and FLETCHER W. S. (1963) A clinical study of primary carcinoma of the gallbladder. *Surg. Gynecol. Obstet.* **117**, 297–300.

COMFORT M. W., GRAY H. K. and WILSON J. M. (1948) Silent gallstone—a 10 to 25 years followup study of 112 cases. *Ann. Surg.* **123**, 931–937.

D'AUNOY R., OGDEN M. A. and HALPERT B. (1938) Primary carcinoma of biliary system, clinicopathological analysis of 40 cases. *Surgery* **3**, 670–678.

FAHIM R. B., MCDONALD J. R., RICHARD J. C. and FERRIS D. O. (1962) Carcinoma of the gallbladder—a study of its mode of spread. *Ann. Surg.* **156**, 114–124.

GRADISAR I. A. and KELLY T. R. (1970) Primary carcinoma of the gallbladder. *Arch. Surg.* **100**, 232–235.

HART J., MODAN B. and SHANI M. (1971) Cholelithiasis in the aetiology of gallbladder neoplasms. *Lancet* **1**, 1151–1153.

HOLMES S. L. and MARK J. B. D. (1971) Carcinoma of the gallbladder. *Surg. Gynecol. Obstet.* **133**, 561–564.

LITWIN M. S. (1967) Primary carcinoma of the gallbladder: a review of 78 patients. *Arch. Surg.* **95**, 236–240.

MACHADO A. L. (1971) Percutaneous transhepatic cholangiography. *Br. J. Surg.* **58**, 616–624.

MCLAUGHLIN C. W. jun. (1964) Carcinoma of the gallbladder: an added hazard in untreated calculous cholecystitis in older patients. *Surgery* **56**, 757–759.

MUSSER J. H. (1889) cited by SOLAN M. J. and JACKSON B. T. (1971).

NIELD J. M. (1964) Primary carcinoma of the gallbladder. *Aust. NZ. J. Surg.* **34**, 43–46.

PEMBERTON L. B., DIFFENBAUGH W. F. and STROHL E. L. (1971) The surgical significance of carcinoma of the gallbladder. *Am. J. Surg.* **122**, 381–383.

ROBERTSON W. A. and CARLISLE B. B. (1967) Primary carcinoma of the gallbladder: review of 52 cases. *Am. J. Surg.* **113**, 738–742.

RUDOLPH R. and COHEN J. J. (1972) Cancer of the gallbladder in an 11 year old Navajo girl. *J. Pediatr. Surg.* **7**, 66–67.

SAMUEL E. (1966) Radiology of the gallbladder. In: ROB C., SMITH R. and MORGAN C. N. (ed.) *Clinical Surgery: Vol.* 10, *Abdomen and Rectum and Anus.* London, Butterworths, pp. 326–333.

SATO T., WATANABE K., SAITOH Y., KOYAMA K. and SUDA Y. (1969) Selective arteriography for gallbladder diseases. Evaluation with reference to carcinoma of the gallbladder. *Arch. Surg.* **99**, 598–605.

SOLAN M. J. and JACKSON B. T. (1971) Carcinoma of the gallbladder—a clinical appraisal and review of 57 cases. *Br. J. Surg.* **58**, 593–597.

STRAUCH G. O. and PROVIDENCE R. I. (1960) Primary carcinoma of the gallbladder. *Surgery* **47**, 368–383.

TANGA M. R. and EWING J. B. (1970) Primary malignant tumours of the gallbladder—report of 43 cases. *Surgery* **67**, 418–426.

WARREN R. and BLACH F. C. (1940) Carcinoma of the gallbladder—the etiological role of gallstones. *Surgery* **7**, 657–666.

Br. J. Surg. Vol. 62 (1975) 37–44

The natural and unnatural history of pancreatic pseudocysts

S. SANKARAN AND ALEXANDER J. WALT*

SUMMARY

Experience with 131 pseudocysts of the pancreas in 112 patients has been analysed with a view to answering specific questions. Spontaneous regression was documented in 8 per cent. Complications occurred in 33·5 per cent of the pseudocysts, including obstruction of adjacent organs, rupture, haemorrhage and pancreatic ascites. In 14 pseudocysts, rupture into the gastrointestinal tract, the peritoneal cavity or the pleural cavity, when unassociated with haemorrhage, had a mortality rate of 14 per cent. Sixteen patients with significant haemorrhage associated with a pseudocyst had a mortality rate of 61 per cent; early direct surgical control is advocated. Pancreatic ascites was associated with 14·5 per cent of the pseudocysts and had a 40 per cent recurrence rate, which can be greatly diminished when operative procedures are guided by pancreatography. The mortality rate for the surgical treatment of 97 uncomplicated pseudocysts was 6 per cent and the recurrence rate was 11 per cent. The prime cause of death was haemorrhage. Seven of the 131 pseudocysts were synchronous and 12 were metachronous. The actual figure is probably higher. Small cysts of the head of the pancreas, impalpable at operation but demonstrable by pancreatography, may be the cause of severe, continuing or recurrent symptoms.

PSEUDOCYSTS of the pancreas often present many difficult clinical problems. In the past, considerable attention has been focused on the management of mature uncomplicated pseudocysts of the pancreas and satisfactory guidelines have emerged from several large studies (Warren et al., 1958, 1966; Becker et al., 1968; Rosenberg et al., 1969). Less definitive information is available on the surgical dilemmas posed by pseudocysts with complications such as rupture, haemorrhage, ascites and recurrence. Furthermore, the symptoms arising from immature and clinically impalpable pseudocysts are frequently not appreciated. With a view to refining our own approach, we have sought the answers to the following questions:

1. What is the natural history of pancreatic pseudocysts?
2. Do they regress spontaneously?
3. What are the hazards of watchful waiting for a pseudocyst to mature?
4. How is rupture of a pseudocyst best treated?
5. How is massive bleeding associated with a pseudocyst best treated?
6. What is the significance of pancreatic ascites?
7. Can symptomatic pseudocysts be impalpable even at laparotomy?
8. How often are pseudocysts multiple?

Material

The records of 112 patients with 131 pancreatic pseudocysts admitted to the Wayne State University Affiliated Hospitals (Detroit General Hospital, Allen Park V. A. Hospital and Harper Hospital) during the period 1960–72 were analysed. Twelve patients were hospitalized twice for the treatment of pancreatic pseudocysts and 7 other patients had two pseudocysts each, detected at the same laparotomy.

Seventy-five per cent of the patients were in the fourth and fifth decades. The age of the patients ranged from 16 to 79 years with a mean age of 41 years. Eighty-six patients were men and 26 patients were women.

Table I: AETIOLOGY OF PANCREATIC PSEUDOCYSTS

Aetiology	No. of patients	No. of cysts
Pancreatitis		
Alcohol	81	99*
Cholelithiasis	5	5
Alcohol+cholelithiasis	14	14
Postrenal transplantation	1	2
Pancreatic trauma	11	11
Total	112	121

* Includes 7 double cysts and 11 recurrent cysts.

Table II: SYMPTOMS AND SIGNS

Symptoms and signs	No. of admissions with symptom or sign present	Frequency in determinate cases (%)*
Pain	107	94
Nausea and vomiting	68	60
Anorexia	25	20
Weight loss (over 4·5 kg)	51	47
Diarrhoea	8	10
Fever	15	21
Mass	62	50
Tenderness	57	72
Ascites	22†	18
Jaundice	10	8
Paroxysmal hypertension	36	49

* Cases in which the finding or its absence was mentioned.
† In 3 instances ascites was due to cirrhosis.

Aetiology (*Table I*)

The development of a pseudocyst was preceded by pancreatitis (90 per cent) or pancreatic trauma (10 per cent). Alcoholism was the principal cause of pancreatitis in our patients. In none of the 19 patients with cholelithiasis was a stone detected in the common

---

* Department of Surgery, Wayne State University School of Medicine, Detroit, Michigan 48201, and Detroit General Hospital, Detroit, Michigan 48226, USA.
Reprint requests to A. J. Walt.

Table III: LABORATORY AND RADIOGRAPHIC FINDINGS

Laboratory and radiographic findings	No. of admissions with test abnormal	Frequency in determinate cases (%)*
Haemoglobin <10 g/100 ml	17	23
Leucocytosis $>12\ 000/\text{mm}^3$	54	48
Serum amylase >200 Somogyi units	85	73
Serum bilirubin elevation (>2 mg/100 ml)	14	13
Carbohydrate metabolic defect	32	35
Pulmonary and/or pleural disease	27	25
Elevation of left diaphragm only	5	5
Pancreatic calcification	8	13
Mass in the region of the pancreas by:		
Upper gastro-intestinal series	89	73
Barium enema	9	36
Intravenous pyelogram	9	36
Arteriogram	7	70

* Cases in which the results of the test were available.

Table IV: LOCATION OF PSEUDOCYSTS

	Location	No. of cysts
Single cysts (105 patients)*	Head	28
	Body/tail	88
	Unknown	1
Double cysts (7 patients)	Head	2
	Body/tail	4
	Head and body/tail	8

* Twelve of these patients had recurrent cysts.

bile duct. One patient was a renal transplant recipient on steroids and azathiaprine; she was also hypercalcaemic. Eleven pseudocysts followed pancreatic trauma. Six patients gave a history of blunt trauma to the abdomen and 5 had been treated for penetrating wounds of the pancreas in the 4 months immediately preceding the development of the pseudocysts.

Symptoms and signs (*Table II*)
Most patients had pain in the upper abdomen ranging from discomfort to severe pain with or without radiation to the back. Weight loss when present was often striking and some patients had lost as much as 18 kg in 3 months. A mass was palpable in only half the cases. Twenty-two patients had chronic ascites; in 19 the ascites appeared to be due to pancreatic leakage in that the fluid contained abnormally raised amylase and protein levels, while in the remaining 3 the ascites was attributable to an associated cirrhosis of the liver. Transient hypertension was noted in 35 patients. This hypertension disappeared when the pseudocysts were adequately drained. The cause of this hypertension is unknown but may conceivably be related to the associated pancreatitis.

Laboratory and radiographic findings (*Table III*)
Twenty-three per cent of the patients were anaemic on admission; most appeared malnourished. None of these patients gave a history of haematemesis or melaena. Leucocytosis was present during the first few days of the hospital stay in 48 per cent of the patients. In many the leucocyte count fell to normal levels prior to surgical therapy. Results of culture of the pseudocyst fluid were available in 30 patients; in 5 the cultures were positive. No correlation was apparent between positive culture of the pseudocyst fluid and the presence of fever or leucocytosis or both preoperatively. The serum amylase was raised during the hospital course in only 73 per cent of determinate cases and often showed marked fluctuations. Elevated serum bilirubin levels were noted in 14 patients; in 10 the hyperbilirubinaemia could be attributed to obstruction of the common bile duct by the pseudocyst, while in 4 the jaundice seemed to be due to early cirrhosis of the liver. Pseudocysts of the head of the pancreas were sometimes associated with a raised serum alkaline phosphatase but a normal serum bilirubin. In one such patient the operative cholangiogram showed the pseudocyst greatly stretching the common bile duct and partially obstructing it (*Fig.* 1). Using as criteria for glucose intolerance a fasting blood sugar greater than 110 mg per cent, a 2-hour postprandial blood sugar over 120 mg per cent or an abnormal glucose tolerance test, 32 patients (35 per cent) demonstrated abnormalities of carbohydrate metabolism.

Radiographic studies demonstrated a mass in the region of the pancreas in only 75 per cent of the cases. In 3 patients the mass was detectable only on the intravenous pyelogram. Twenty-five per cent of the patients had unilateral or bilateral pleural effusion with or without atelectasis or pneumonia in the lower lung fields. Five others had an elevated left diaphragm as the only abnormality on the chest X-rays. Abdominal X-rays showed pancreatic calcification in 13 per cent of determinate cases; each of these patients had an abnormally raised serum amylase. Plain films of the abdomen sometimes showed non-specific ileus, ascites or findings suggestive of a mass.

Location of pseudocysts (*Table IV*)
Seven patients had two pseudocysts at the same laparotomy. In each, pancreatitis was associated with excessive alcoholic intake. Thirty-four pseudocysts (26 per cent) were located in the head of the pancreas. Twelve of these (30 per cent) caused significant obstruction of the common bile duct or duodenum. Ten patients had jaundice from obstruction of the common bile duct. The elevations in serum bilirubin were between 3 and 5 mg per cent in 4 patients, between 10 and 15 mg per cent in 2 patients and over 15 mg per cent in 3 patients. In 2 patients rupture of the cysts into the duodenum and duodenum and common bile duct respectively was demonstrated radiologically concomitant with the regression of jaundice.

Natural and unnatural history
Forty of the 131 pseudocysts either regressed spontaneously or were associated with one or more complications—rupture, haemorrhage or ascites—

before any operation was performed. Non-operative treatment was deliberately chosen in only one patient owing to her poor respiratory function from previous pulmonary tuberculosis and a thoracoplasty. The cyst in the tail of her pancreas was confirmed by a selective splenic arteriogram. For the past 1½ years she has been followed as an outpatient and has been taking simple analgesics periodically. She has abstained from alcohol and her weight has been stable at around 44 kg.

Spontaneous regression

Spontaneous regression of a pseudocyst was observed in 10 patients. In 3 of these, spontaneous drainage of the cyst into the duodenum (*Fig*. 2), duodenum and common bile duct (*Fig*. 3) and colon (*Fig*. 4) respectively was radiologically demonstrated. In another unusual

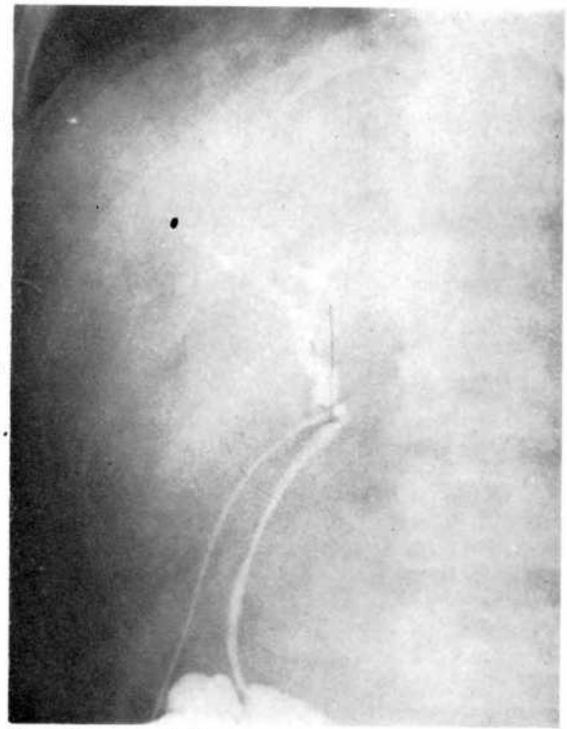


Fig. 1. Operative cholangiogram showing a pseudocyst greatly stretching and partially obstructing the common bile duct.

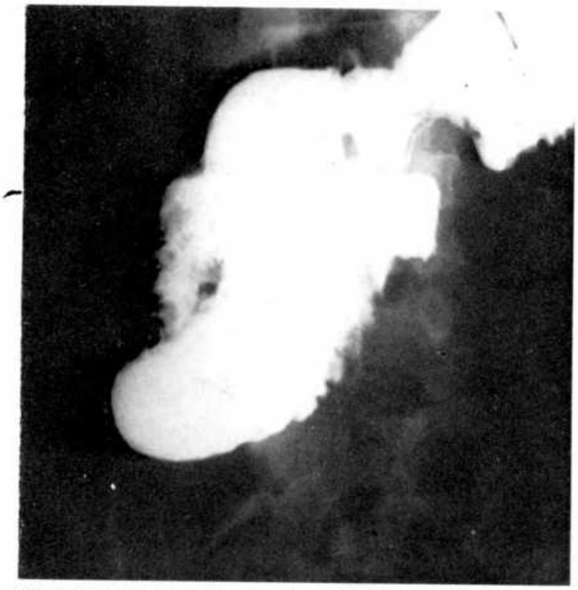


Fig. 2. Barium meal film showing a fluid level following rupture of a pseudocyst into the duodenum with spontaneous regression.

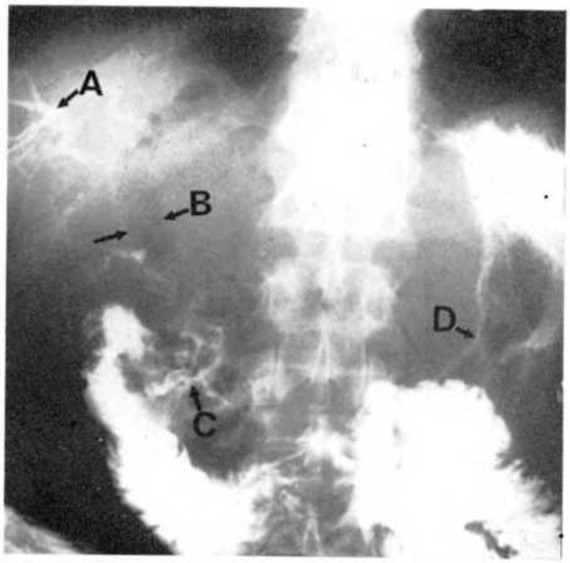


Fig. 3. Barium meal film showing barium in the cyst cavity (C) and in the biliary tree (A, B). A second pseudocyst (D) can be seen displacing the stomach to the left.

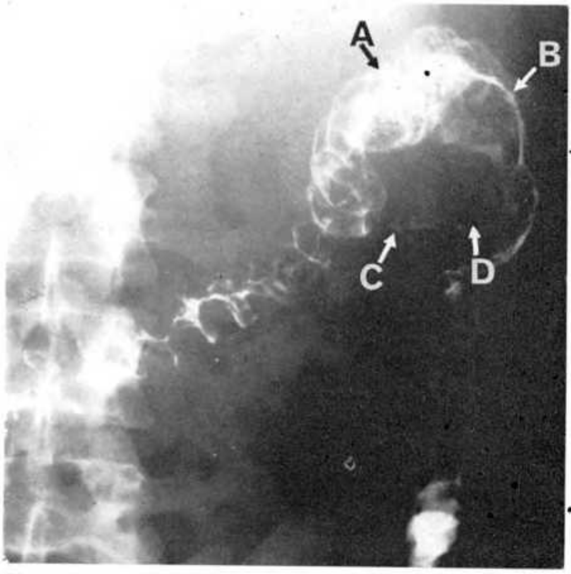


Fig. 4. Barium film showing rupture of a pseudocyst (A, B, C, D) into the splenic flexure of the colon with spontaneous regression.

Table V: PSEUDOCYSTS OF THE PANCREAS WITH PREOPERATIVE COMPLICATIONS

Treatment	Pancreatic ascites only	Acute cyst rupture only	Cyst with haemorrhage only	Cyst with rupture and haemorrhage	Cyst with rupture and ascites	Cyst with ascites and haemorrhage	Total
Non-surgical	1	2		1			4
	1						1
					1		2
Exploratory laparotomy		1			1		2
	2				2		4
External drainage	4	5	1	1	2	2	15
		2	1			2	5
Cystoduodenostomy	1						1
	1						1
Cystogastrostomy	6						6
	1						1
Cystojejunostomy					1		1
Excision, distal pancreatectomy and splenectomy	1	2		2			5
				1			
	3				3		6
Total	13	10	1	4	4	2	34
	2	2	1	1		2	8

Upper right corner, Number of recurrences (cyst, ascites or both). Lower right corner, Number of deaths.

Table VI: PSEUDOCYSTS WITH RUPTURE AND HAEMORRHAGE: RESULTS OF TREATMENT

	No. of cysts	Mortality rate (%)
Acute rupture without haemorrhage	14	14
Massive haemorrhage with or without rupture	7	57
Total	21	29 ($P<0.005$)

Table VII: SITE OF RUPTURE OF PANCREATIC PSEUDOCYSTS

Site of rupture	No. of cysts* (20)
Peritoneal cavity	7
Stomach and peritoneal cavity	1
Splenic artery and peritoneal cavity	1
Mediastinum and right pleural cavity	3
Oesophagus	1
Stomach	1
Duodenum	4
Colon	1
Spleen	1

* One cyst ruptured into the stomach and peritoneal cavity and another cyst ruptured into the duodenum and common bile duct.

Table VIII: TIME OF RUPTURE OF PANCREATIC PSEUDOCYSTS

Time of rupture	No. of cysts (20)
On admission	4
First week	6
Second week	7
After 4 weeks	3

patient the pseudocyst regressed and reappeared repeatedly, depending upon whether the patient was recumbent or in the upright position. In the remaining 6 patients, spontaneous regression of a pseudocyst was inferential; a mass with all the classic features of a pseudocyst, demonstrated by palpation and radiological studies, disappeared as the patient became asymptomatic.

Pseudocysts with preoperative complications

Thirty-four pseudocysts (26 per cent) in 33 patients developed one or more complications preoperatively (*Table V*). Eight patients with these complications died and 6 had a recurrence of a pseudocyst or ascites or both. In the patients whose pseudocyst (21) ruptured or bled before operation the mortality was high (*Table VI*). All 6 patients with a recurrence had pancreatic ascites preoperatively.

a. Rupture: Twenty pseudocysts in 19 patients ruptured acutely into a variety of adjacent organs and spaces (*Table VII*); 4 of these patients had associated pancreatic ascites, another 4 had associated massive haemorrhage and 2 had both ascites and massive haemorrhage. The time of rupture was unpredictable (*Table VIII*). Only one of the ruptured pseudocysts, operated on 4 weeks after rupture, had walls thick enough for internal drainage.

Seven patients had acute rupture of their pseudocyst into the peritoneal cavity with signs and symptoms of peritonitis. In one of these the rupture followed haemorrhage from the splenic artery into the pseudocyst, and in another the cyst had also eroded into the stomach. Rupture of a pseudocyst into the mediastinum and right pleural cavity occurred via the oesophageal hiatus in 2 cases and the aortic hiatus in 1. Of the 8 patients in whom pseudocysts ruptured into the gastro-intestinal tract, 4 had associated massive upper gastro-intestinal bleeding. The source of bleeding was the left gastric artery in the pseudocyst that ruptured into the oesophagus and the gastroduodenal artery in the 2 cysts that ruptured into the duodenum; in the fourth patient the bleeding ceased

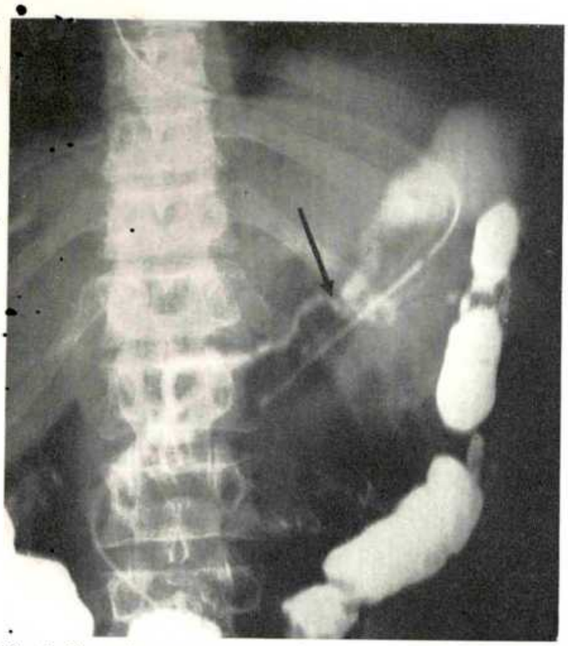


Fig. 5. Operative pancreatogram in a patient with pancreatic ascites showing leakage of contrast medium from the pancreatic duct into a pseudocyst which was leaking.

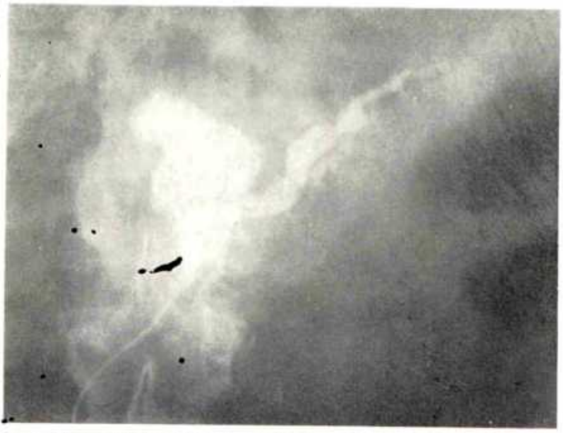


Fig. 6. Operative pancreatogram showing a pseudocyst in the head of the pancreas which has ruptured into the right pleural cavity.

of the pseudocyst preoperatively and died of sepsis, while the fourth died of massive bleeding 6 hours after cystogastrostomy. Six patients (40 per cent) had a recurrence of a pseudocyst or ascites or both. One recurrence followed laparotomy and peritoneal lavage in a patient whose pseudocyst had ruptured into the peritoneal cavity; 4 other recurrences followed external drainage alone.

Uncomplicated pseudocysts

Ninety-seven pseudocysts in 79 patients developed no preoperative complications such as ascites, rupture or haemorrhage. *Table XII* details the management and results of therapy.

Table XI: PANCREATIC ASCITES (19 CASES)

	No. of cases:
Palpable mass	2 (11%)
Mass demonstrated radiographically	10 (53%)
Recurrence	7 (40%) ($P < 0{\cdot}002$)

Table XII: RESULTS OF TREATMENT OF UNCOMPLICATED PSEUDOCYSTS

Treatment	No. of cysts	Mortality rate (%)	Recurrence (rate %)
Non-operative	8	0	12·5
External drainage	18	5·5	17
Transduodenal aspiration of cyst	2	0	0
Cystoduodenostomy	8	0 }	0 }
Cystogastrostomy	25	8 } 5	8 } 11
Cystojejunostomy	23	4 }	17 }
Excision and partial pancreatectomy	13	18	0
Total	97	6	11

Six patients died. One patient who was progressing satisfactorily after distal pancreatectomy and splenectomy died of massive pulmonary embolism on the eighth postoperative day. A second patient died postoperatively of renal failure after the same procedure. The remaining 4 deaths were associated with post-operative bleeding after external drainage in 1 patient, after cystogastrostomy in 2 patients and after Roux-en-Y cystojejunostomy in 1 patient. All 4 were treated non-operatively. Non-fatal complications post-operatively included prolonged pancreatitis in 2 patients, left subphrenic abscess in 1 and upper gastro-intestinal bleeding in 1 which ceased spontaneously after transfusion of 7 units of blood.

From *Table XI* it will be noted that 2 patients had transduodenal aspiration of the cyst only. The capacity of these two cysts was only 10 and 30 ml respectively. Both had severe and persistent symptoms and slight widening of the duodenal sweep on upper gastro-intestinal radiographic series, and became asymptomatic postoperatively. Neither patient had a pancreatogram. One other patient with persistent upper abdominal pain and hyperamylasaemia, whose pancreas had been explored 18 months earlier for similar symptoms, had no demonstrable mass in the region of the pancreas by upper gastro-intestinal radiographic series or by palpation at laparotomy. A transduodenal pancreatogram, however, demonstrated a pseudocyst in the head of the pancreas. A cystoduodenostomy was performed with excellent clinical results.

Recurrent and/or new pseudocysts (*Table XII*)

Fourteen patients had recurrence of a pseudocyst and 2 had recurrence of pancreatic ascites without a pseudocyst. Two of the recurrent pseudocysts were treated elsewhere and are not included in *Table XII*. The second pseudocyst was located at a site different from the first in only 3 patients. In 5 of the remaining 9 patients, pancreatic ascites was associated with the first pseudocyst. It is purely speculative whether the recurrences were due to (*a*) inadequate therapy of the

Table IX: PREOPERATIVE HAEMORRHAGE

Clinical manifestation of bleeding	Source	Treatment	Results
Upper gastro-intestinal	Left gastric artery	Ligation+external drainage	Died
	Gastroduodenal artery	Ligation+external drainage	Died
	Gastroduodenal artery	Ligation+external drainage	Satisfactory
	Unknown	6 Units of blood	Satisfactory
	Unknown	4 Units of blood+external drainage	Ceased. Re-bled post-operatively. Died
Intracystic	Splenic artery	Ligation+distal pancreat-ectomy and splenectomy	Satisfactory
	Spleen	Ligation+distal pancreat-ectomy and splenectomy	Died

Table X: POSTOPERATIVE HAEMORRHAGE

Initial treatment	Clinical manifestation of bleeding	Source	Treatment	Results
External drainage	Intracystic	Unknown	Non-operative	Died
	External	Cyst wall	Pancreatoduodenectomy	Died
	External	Cyst wall	Packing	Died
	External	Cyst wall	Non-operative	Died
	External	Cyst wall	Non-operative	Survived
	External	Erosion of sump drain into splenic artery	Ligation of bleeder	Survived
Cystogastrostomy	Upper gastro-intestinal	Anterior gastrotomy wound	Ligation of bleeder	Survived
	Upper gastro-intestinal	Unknown	Non-operative	Died
	Upper gastro-intestinal	Unknown	Non-operative	Survived
	Intracystic	Cyst wall	Non-operative	Died
Cystojejunostomy		Suture line leak and bleeding	Non-operative	Died

spontaneously and no specific source was identified at subsequent laparotomy.

Two patients became completely asymptomatic following rupture of the pseudocyst into the duodenum and colon respectively. The 3 patients who had rupture of a pseudocyst into the mediastinum and right pleural cavity improved temporarily after removal of the pleural fluid but subsequently needed surgical drainage of the pseudocyst. Most patients with rupture of a pseudocyst into the peritoneal cavity or with associated massive haemorrhage required vigorous intravenous replacement and urgent laparotomy.

At laparotomy in 2 patients the peritoneal cavity was lavaged but the collapsed pseudocyst was not drained; both patients survived but one developed a recurrent pseudocyst. In 10 patients the pseudocyst was drained externally; 4 died. Two patients had associated preoperative massive gastro-intestinal bleeding and died of sepsis, a third died of postoperative bleeding and sepsis and the fourth died of respiratory failure 3 days postoperatively. One of the patients with rupture of the pseudocyst into the right pleural cavity developed chronic pleural effusion and pancreatic ascites but became well following Roux-en-Y cystojejunostomy. Four patients had distal pancreatectomy and splenectomy without recurrence; one in whom the pseudocyst had ruptured into the spleen died of sepsis. Excluding the 6 patients with associated preoperative bleeding (3 of whom died), only 2 of 14 patients with acute rupture of a pseudocyst died—one of respiratory failure and the other of postoperative bleeding and sepsis.

b. Haemorrhage (*Tables IX, X*): Massive haemorrhage with a pseudocyst is an unpredictable serious complication. Four of 7 patients (57 per cent) with preoperative bleeding and 7 of 11 patients (64 per cent) with postoperative bleeding died. One patient bled both pre- and postoperatively. This complication is the prime cause of mortality in our patients with pseudocysts of the pancreas; 10 of 14 patients in the entire series who died bled either pr[illegible]or postoperatively. The remaining deaths were due to massive pulmonary embolism in 2, acute respiratory failure in the third and renal failure in the fourth.

c. Pancreatic ascites (*Table X*): Eighteen patients had 19 episodes of pancreatic ascites. The diagnosis of pancreatic ascites was based on chronic ascites with the triad of elevated serum amylase, elevated ascitic fluid amylase (346–97 000 Somogyi units/100 ml) and elevated ascitic fluid proteins (2·5–5·5 g/100 ml). A pseudocyst was palpable in only 2 patients, even after paracentesis, and radiographically demonstrable in only 10. In 2 cases a mass was not palpable even at laparotomy but intra-operative pancreatography revealed the pseudocyst (*Figs*. 5, 6). The patient whose pancreatogram is depicted in *Fig*. 6 is of special interest as he also had chronic pancreatic pleural effusion subsequent to rupture of the pseudocyst into the mediastinum and right pleural cavity. Following a Roux-en-Y cystojejunostomy of the abdominal portion of the pseudocyst, his pleural effusion disappeared in a few days. *Table V* details the types of treatment given and the results. Of the 4 patients who died, 1 had massive pulmonary embolism before operation, 2 patients had massive bleeding and rupture

Table IX: PREOPERATIVE HAEMORRHAGE

Clinical manifestation of bleeding	Source	Treatment	Results
Upper gastro-intestinal	Left gastric artery	Ligation + external drainage	Died
	Gastroduodenal artery	Ligation + external drainage	Died
	Gastroduodenal artery	Ligation + external drainage	Satisfactory
	Unknown	6 Units of blood	Satisfactory
	Unknown	4 Units of blood + external drainage	Ceased. Re-bled postoperatively. Died
Intracystic	Splenic artery	Ligation + distal pancreatectomy and splenectomy	Satisfactory
	Spleen	Ligation + distal pancreatectomy and splenectomy	Died

Table X: POSTOPERATIVE HAEMORRHAGE

Initial treatment	Clinical manifestation of bleeding	Source	Treatment	Results
External drainage	Intracystic	Unknown	Non-operative	Died
	External	Cyst wall	Pancreatoduodenectomy	Died
	External	Cyst wall	Packing	Died
	External	Cyst wall	Non-operative	Died
	External	Cyst wall	Non-operative	Survived
	External	Erosion of sump drain into splenic artery	Ligation of bleeder	Survived
Cystogastrostomy	Upper gastro-intestinal	Anterior gastrotomy wound	Ligation of bleeder	Survived
	Upper gastro-intestinal	Unknown	Non-operative	Died
	Upper gastro-intestinal	Unknown	Non-operative	Survived
	Intracystic	Cyst wall	Non-operative	Died
Cystojejunostomy		Suture line leak and bleeding	Non-operative	Died

spontaneously and no specific source was identified at subsequent laparotomy.

Two patients became completely asymptomatic following rupture of the pseudocyst into the duodenum and colon respectively. The 3 patients who had rupture of a pseudocyst into the mediastinum and right pleural cavity improved temporarily after removal of the pleural fluid but subsequently needed surgical drainage of the pseudocyst. Most patients with rupture of a pseudocyst into the peritoneal cavity or with associated massive haemorrhage required vigorous intravenous replacement and urgent laparotomy.

At laparotomy in 2 patients the peritoneal cavity was lavaged but the collapsed pseudocyst was not drained; both patients survived but one developed a recurrent pseudocyst. In 10 patients the pseudocyst was drained externally; 4 died. Two patients had associated preoperative massive gastro-intestinal bleeding and died of sepsis, a third died of postoperative bleeding and sepsis and the fourth died of respiratory failure 3 days postoperatively. One of the patients with rupture of the pseudocyst into the right pleural cavity developed chronic pleural effusion and pancreatic ascites but became well following Roux-en-Y cystojejunostomy. Four patients had distal pancreatectomy and splenectomy without recurrence; one in whom the pseudocyst had ruptured into the spleen died of sepsis. Excluding the 6 patients with associated preoperative bleeding (3 of whom died), only 2 of 14 patients with acute rupture of a pseudocyst died—one of respiratory failure and the other of postoperative bleeding and sepsis.

b. Haemorrhage (*Tables IX, X*): Massive haemorrhage with a pseudocyst is an unpredictable serious complication. Four of 7 patients (57 per cent) with preoperative bleeding and 7 of 11 patients (64 per cent) with postoperative bleeding died. One patient bled both pre- and postoperatively. This complication is the prime cause of mortality in our patients with pseudocysts of the pancreas; 10 of 14 patients in the entire series who died bled either pre- or postoperatively. The remaining deaths were due to massive pulmonary embolism in 2, acute respiratory failure in the third and renal failure in the fourth.

c. Pancreatic ascites (*Table X*): Eighteen patients had 19 episodes of pancreatic ascites. The diagnosis of pancreatic ascites was based on chronic ascites with the triad of elevated serum amylase, elevated ascitic fluid amylase (346–97 000 Somogyi units/100 ml) and elevated ascitic fluid proteins (2·5–5·5 g/100 ml). A pseudocyst was palpable in only 2 patients, even after paracentesis, and radiographically demonstrable in only 10. In 2 cases a mass was not palpable even at laparotomy but intra-operative pancreatography revealed the pseudocyst (*Figs*. 5, 6). The patient whose pancreatogram is depicted in *Fig*. 6 is of special interest as he also had chronic pancreatic pleural effusion subsequent to rupture of the pseudocyst into the mediastinum and right pleural cavity. Following a Roux-en-Y cystojejunostomy of the abdominal portion of the pseudocyst, his pleural effusion disappeared in a few days. *Table V* details the types of treatment given and the results. Of the 4 patients who died, 1 had massive pulmonary embolism before operation, 2 patients had massive bleeding and rupture first pseudocyst, (*b*) failure to detect a second pseudocyst or source of leakage from the pancreatic ductal system at the first operation or (*c*) formation of a new pseudocyst.

Discussion

Pseudocysts of the pancreas are collections of fluid and debris, rich in pancreatic enzymes, in the region of the pancreas or within its parenchyma. In contrast to true cysts, pseudocysts do not have an epithelial lining and disruption of the pancreatic ductal system is a prerequisite. The subsequent course of this disruption, however, may vary widely from spontaneous healing to continuous leakage of pancreatic juice causing tense abdominal distension due to pancreatic ascites. Between these extremes, pseudocysts may form and these in turn may occasionally regress spontaneously by decompression into a pancreatic duct or into an adjacent organ. In a few cases in our series, cure followed radiologically demonstrated rupture into the common bile duct, duodenum or transverse colon. It is probable that such communications may also develop between the pseudocyst and other organs such as the stomach or small intestine. Eight per cent of our 131 pseudocysts regressed spontaneously; this is, in all likelihood, a minimal figure.

Despite the evidence of spontaneous regression, conservative non-surgical treatment is not advocated because of the frequency, unpredictability and severity of the potential complications associated with pseudocysts. Of our 131 pseudocysts, 42 (33·5 per cent) obstructed the duodenum or common bile duct, ruptured, leaked or bled. These hazards are more likely to occur during the immature phase of the development of the pseudocyst when the walls are tenuously formed by adjacent organs and peritoneal structures. This temporal relationship has considerable relevance in the debate concerning the advisability of urgent surgical operation to forestall the development of a cyst wall thick enough to permit safe internal anastomosis. Of the 20 pseudocysts which ruptured in our series, 17 did so within 4 weeks (*Table VIII*). In only 1 of these 20—a pseudocyst known to have been present for 4 weeks—was internal drainage thought to be feasible. These findings suggest that patients with suspected pancreatic pseudocysts should be kept under very close observation if the decision is made to delay surgery. We prefer to operate on mature pseudocysts and consequently keep these patients with fresh pseudocysts in hospital away from alcohol for 2–4 weeks during this phase of preoperative preparation. A number who continue to be symptomatic and are unable to eat adequately are helped by intravenous hyperalimentation.

Rupture into the peritoneal cavity and haemorrhage are the principal causes of death attributable to pseudocysts. Our experience of acute rupture into the peritoneal cavity has been more encouraging than is usually stated (Hanna, 1960), as only 1 of 7 patients died. In contrast, the results of haemorrhage have been dismal, 61 per cent of these patients dying (*Tables IX, X*). While an occasional patient may stop bleeding spontaneously, the chance of this occurring is unpredictable. Although 3 of 10 bleeding patients in whom no definitive procedure was done survived, it was apparent on critical review of the deaths that a number may well have been saved if early surgery had been instituted. From these experiences, a policy of rapid surgical intervention, even in apparently adverse circumstances, is now advocated for all patients with pseudocysts who have associated significant bleeding.

Pancreatic ascites is a much more common complication than reported in the past, occurring in 19 of our 131 pseudocysts (14·5 per cent), and must always be considered when an alcoholic patient develops fluid in the peritoneal cavity. The associated pseudocysts may be very difficult to demonstrate radiologically or clinically in these patients, even after paracentesis (*Table XI*), and may only be demonstrable at operation. We have also demonstrated the presence of a pseudocyst in such a patient preoperatively by pancreatography performed after cannulation of the pancreatic duct through a fibre-optic duodenoscope. Newer techniques, including sonagrams, may make future treatment more accurate. Recurrence of pseudocysts associated with pancreatic ascites has been inordinately high (40 per cent) in this series, but more recently, with specific delineation of the source of leakage and a knowledge of the ductal system gained through pancreatography performed at operation, successful definitive surgery has been the rule rather than the exception. Where the leak is associated with an immature pseudocyst or when no obvious pseudocyst is present, pancreatography is advisable. When distal pancreatectomy is performed, antegrade pancreatography is necessary to help in the determination of whether a more proximal ductal stenosis makes distal pancreaticojejunostomy (rather than simple ligation of the duct) essential. If the leak is identified in the wall of a mature pseudocyst, internal drainage is effective.

As more frequent pancreatography and more extensive exploration of the pancreas have been carried out, two important observations made by others have been confirmed. Anderson (1972) has pointed out that 23 per cent of the pseudocysts in his series were multiple. While the overall incidence of multiplicity was only 6 per cent in our series, the frequency of detection of more than one cyst has risen in recent years. Continuing symptoms following apparently adequate drainage of a well-defined pancreatic pseudocyst is sometimes due to failure to recognize a concomitant cyst at the first operation (*Table XII*). Secondly, severe symptoms of recurrent or persistent pancreatitis may be present when no pseudocyst can be delineated on a radiographic gastro-intestinal series or palpated in the pancreas, even at operation (Nardi et al., 1969). Retrograde pancreatography is essential in these circumstances as, apart from aspiration, this may be the only method of detecting the pseudocyst which may either fill with radio-opaque material or distort the pancreatic ductal system. The area of the head of the pancreas drained by the duct of Santorini has not been given the attention which it deserves (Anderson, 1972). Small cysts in this region may be strategically placed to produce obstruction of the common bile duct, bleeding from the gastroduodenal artery and severe continuing symptoms. In 2 cases where internal drainage was not performed, simple aspiration of 10 and 35 ml of fluid respectively rendered the patients asymptomatic.

Our most satisfactory results in pseudocysts of the head of the pancreas have been obtained by cystoduodenostomy where this has been feasible. In pseudocysts of the body and tail cystogastrostomy and cystojejunostomy produced comparable results. Cystogastrostomy, being quicker and easier, seems more desirable when the posterior wall of the stomach is adherent to the pseudocyst. Despite speculation that alkaline pancreatic secretions may bathe the antrum and stimulate the production of gastric acid to the point of causing gastroduodenal erosions or ulcerations, we have not encountered this sequence in practice. If at the time of operation the cyst wall is immature in that it does not lend itself to secure anastomosis, external drainage has been satisfactory. Drainage from the sinus tract may continue for several weeks, and it is essential that the drains are left in place until a well-defined tract has formed. No operation for a chronic pancreatic fistula has been required in this series. The main hazard encountered has been bleeding, possibly due to erosion by a sump tube of an adjacent vessel, and special care must consequently be taken in the selection and placement of drains. Finally, in recent years excision of the body and tail of the pancreas in selected cases (e.g. invasion of the spleen or kidney by the pseudocyst or in cases of bleeding or rupture) has been performed far more readily than in the past. The results of this more aggressive approach have been encouraging.

Acknowledgement
This work was supported by Detroit General Hospital Research Corporation.

References

ANDERSON M. D. (1972) Management of pancreatic pseudocysts. *Am. J. Surg.* **123**, 209–221.

BECKER W. F., PRATT H. S. and GANJI H. S. (1968) Pseudocysts of the pancreas. *Surg. Gynecol. Obstet.* **127**, 744–747.

HANNA W. A. (1960) Rupture of pancreatic cysts. Report of a case and review of the literature. *Br. J. Surg.* **47**, 495–498.

NARDI G. L., LYON D. C., SHEINER H. J. and BARTLETT M. K. (1969) Solitary occult retention cysts of the pancreas. *New Engl. J. Med.* **280**, 11–15.

ROSENBERG I. K., KAHN J. A. and WALT A. J. (1969) Surgical experience with pancreatic pseudocysts. *Am. J. Surg.* **117**, 11–17.

WARREN K. W., ATHANASSIADES S., FREDERICK P. and KUNE G. A. (1966) Surgical treatment of pancreatic cysts of 183 cases. *Ann. Surg.* **163**, 886–891.

WARREN W. D., MARCH W. H. and SANDUSKY W. R. (1958) An appraisal of surgical procedures for pancreatic pseudocyst. *Ann. Surg.* **146**, 903–920.

Br. J. Surg. Vol. 62 (1975) 45–51

The occult osteomatous changes in the mandible in patients with familial polyposis coli

JOJI UTSUNOMIYA AND TADASHI NAKAMURA*

SUMMARY

Characteristic radio-opaque lesions were detected in the mandibular bone, most clearly on the panoramic X-ray, in 27 or 93·2 per cent out of 29 cases in 15 families with familial polyposis coli, including 21 cases without Gardner's stigmata, 7 cases with the incomplete syndrome and 1 with the complete syndrome.

Only 3 out of 19 members of these families who were free from polyposis had radio-opaque jaw lesions. The cases with polyposis of other types also showed a negative result.

The radiological diagnosis suggested that the lesions were of the character of endosteoma. Our observation is considered to be significant evidence in the understanding of the pathogenesis of Gardner's syndrome as well as a useful method for the early detection of carriers in the polyposis family.

THE term 'familial polyposis coli' (FPC) is defined in the present paper to include all the pathological conditions with numerous adenomatous polyps diffusely distributed in most parts of the large intestine regardless of familial occurrence and the association of extracolic lesions.

While studying FPC we have frequently observed minute extracolic neoplastic lesions, including Gardner's stigmata, osteoma (Gardner and Plenk, 1951) and/or soft tissue tumours such as epithelial cyst and fibrous tumours (Gardner and Richards, 1953), on detailed examination or at laparotomy. A thorough review of the world literature revealed a very high incidence of osteoma in the mandible (Chang et al., 1968; Utsunomiya et al., 1972) and the frequent appearance of abnormal dental growth (Fader et al., 1962) in cases which were reported as typical 'Gardner's syndrome' (synonymous with FPC with complete Gardner's syndrome as mentioned later in the present paper). We therefore decided to carry out radiological examination of the oral region on a routine basis in patients diagnosed as having FPC, and observed peculiar radio-opaque lesions detectable only by detailed dentomaxillar radiological examination techniques even in the cases without manifested associated changes.

Patients and methods

The cases submitted for the present study were divided into the following groups.

1. *Polypotic members of FPC families*

This group comprised a total of 29 cases (16 males and 13 females with an average age of 34·1 years) diagnosed as FPC and distributed in 15 independen families. A definite familial distribution has been detected in all but one family as shown in *Fig.* 1.

2. *Non-polypotic members of FPC families*

Nineteen members belonging to 9 of the above families were found to be free from polyposis at examination. They included 5 males and 14 females with an average age of 24·6 years (*Table I*, *Fig.* 1).

3. *Cases with intestinal polyposis of other types*

These included the following cases: 6 cases (3 males and 3 females with an average age of 20 years) of Peutz–Jeghers syndrome which were confirmed by the typical oral and digital pigmentation and scattered gastro-intestinal polyposis (Jeghers et al., 1949) with hamartomatous histological findings (Bartholomew et al., 1957); 1 male aged 33 years who was diagnosed as having juvenile polyposis coli by the characteristic histological findings as described by Veale et al. (1966); 4 males, with an average age of 58 years, who had several adenomatous polyps in the colon and rectum without familial occurrence.

Routine medical examination of all the cases was done, with particular emphasis being placed on radiology of the gastro-intestinal tract, fibrescopy of the stomach and colon, palpation and inspection of the body surface, systemic bone survey and anamnesis of tumour removal.

All these patients received routine dental and oral radiological examinations including craniography and intra-oral, mandibular body and panoramic radiography.

Medical findings

Colons removed from 23 patients revealed typical features, mostly of rather small, sessile adenomas diffusely distributed throughout the specimens, as seen in *Fig.* 2 which shows typical specimens from 3 members of family T78. Solitary or multiple malignant lesions were found in 10 patients. The remaining 5 non-operated patients showed characteristic radiological and endoscopic features of diffuse polyposis coli.

The associated neoplastic lesions were detected in diverse anatomical sites other than the gastro-intestinal tract, as listed in *Table I*. The patients were classified regarding the extracolic Gardner's stigmata, including osteoma and soft tissue tumours, into the following

---

* Second Department of Surgery, Medical School, and Department of Radiology, Dental School, Tokyo Medical and Dental University.

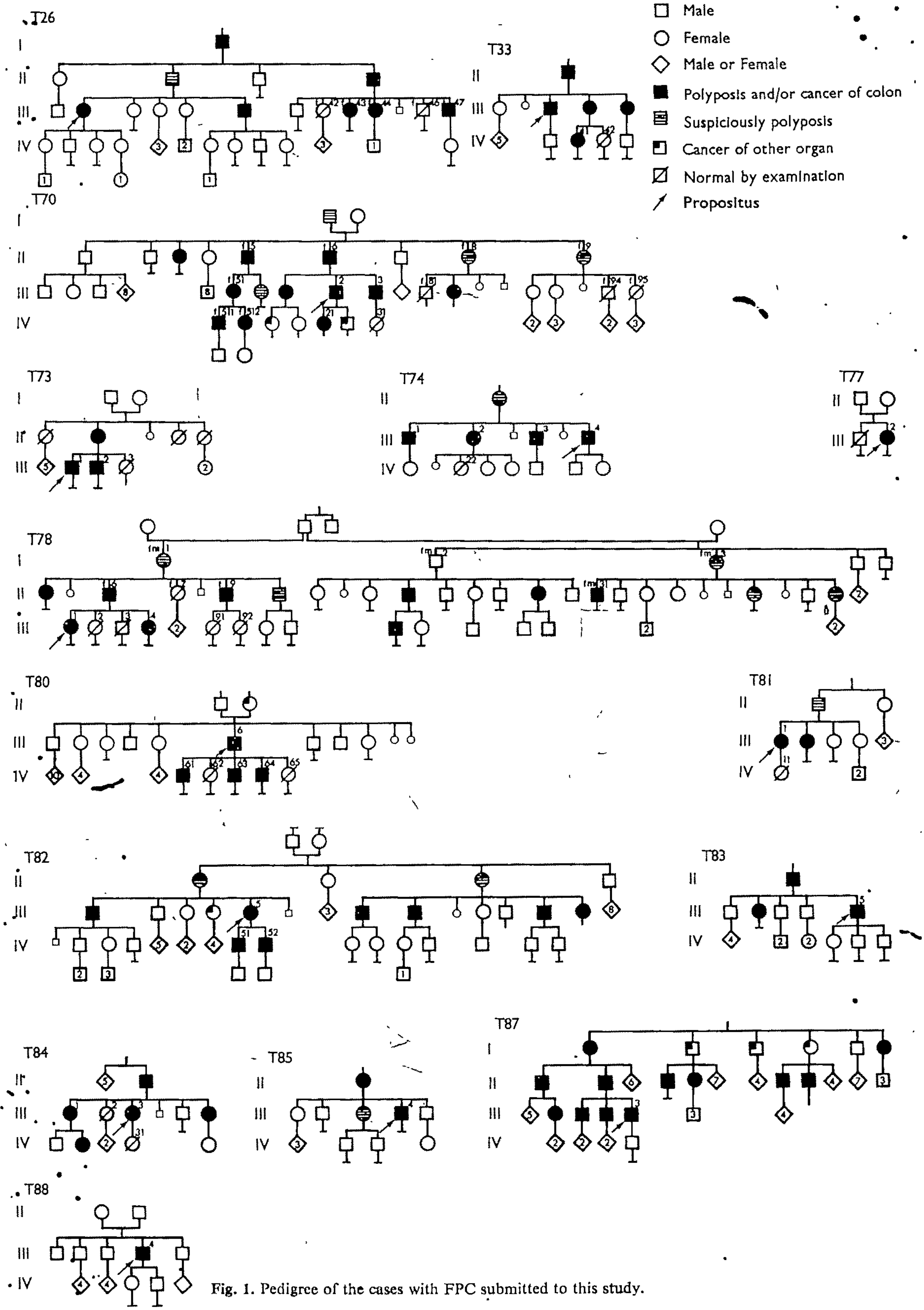


Fig. 1. Pedigree of the cases with FPC submitted to this study.

Table I: SUMMARY OF THE FINDINGS ON PANORAMIC X-RAYS OF THE JAWS OF THE MEMBERS OF POLYPOSIS FAMILIES

Family no.	Case no.	Sex	Age	Mode of diagnosis	'Osteoma' of mandible	Impacted teeth	Neoplastic lesions in other parts of the body
Cases with polyposis							
T26	III-f43	F	38	Op.	+++	–	(B) Fibroma, epithelial cyst
	III-f44	F	36	Op.	++	+	(A) Polyp of the uterus
	III-f47	M	26	Op.	+	–	(A)
T33	IV-41	F	14	Ex.	+++	+	(A)
T70	III-2*	M	47	Op.	++	–	(A) Epithelial cyst 0·7 cm diameter in the neck, osteoma 0·7 cm diameter in the forehead
	III-3	M	43	Op.	+	+	(B) Liver cyst, osteoma 0·7 cm diameter in the forehead and in a metacarpal bone
	IV-21	F	22	Op.	+++	–	(B) Fibroma 1·2 cm diameter in the ovary
	IV-f511	M	24	Ex.	++	+	(A)
	IV-f512	F	19	Op.	+	–	(A)
T73	III-1*	M	22	Op.	+++	–	(B) Cyst 2·0 cm diameter in the arm
T74	III-2*	F	47	Op.	–	–	(A)
T77	III-2*	F	24	Op.	++	+	(A)
T78	II-f6	M	53	Op.	++	+	(A)
	II-fm31	M	53	Ex.	++++	–	(A)
	III-1*	F	26	Op.	++++	–	(A)
	III-4	F	23	Op.	++++	–	(A)
T80	III-6*	M	56	Op.	+	–	(A)
	IV-61	M	27	Op.	+	–	(A)
	IV-62	M	20	Op.	+	+	(A)
	IV-63	M	16	Ex.	++	–	(A)
T81	III-1*	F	41	Op.	+++	+	(B) Fibrous tumour 4·0 cm diameter in the back removed
T83	III-5*	M	41	Op.	++†	+	(C) *See* text
T82	III-5*	F	51	Op.	++	–	(A)
	IV-51	M	30	Ex.	+	–	(A)
T84	III-1	F	36	Op.	++	+	(A)
	III-3*	F	30	Op.	++	–	(B) Cyst 1·2 cm diameter in the leg
T85	III-4*	M	46	Op.	–	–	(A)
T86	III-3*	M	26	Op.	++	+	(B) Small osteoma in the skull
T88	III-3*	M	52	Op.	++	–	(A)
Cases without polyposis							
T26	III-f41	F	40		–	–	
	III-f46	M	30		–	–	
T33	IV-42	F	12		–	–	
T70	IV-31	F	19		–	–	
	III-f81	M	41		–	–	
	III-f94	M	37		–	–	
	III-f95	F	30		–	–	
T74	IV-29	F	20		–	–	
T77	III-1	M	20		–	–	
T78	II-7	F	50		–	–	
	III-2	F	25		+	–	
	III-3	M	23		+	–	
	III-f91	F	17		–	–	
	III-f92	F	13		–	–	
T80	IV-62	F	23		–	–	
	IV-65	F	14		–	–	
T81	IV-11	F	13		+	–	
T84	III-2	F	33		–	–	
	IV-31	F	7		–	–	

* Propositus. † Includes odontomas.
Op., Operated. Ex., Examined by X-ray and endoscope.
'Osteoma': osteomatous changes represented as + single lesion, ++ from two to five lesions, +++ from six to ten lesions, ++++ over eleven lesions.
(A), Simple FPC. (B), FPC with incomplete Gardner's syndrome. (C), FPC with complete Gardner's syndrome.

three groups: simple FPC type including 21 patients in whom the stigmata were not detected; FPC with incomplete Gardner's syndrome including 7 patients who had one of the stigmata or in whom both types were manifested but very slightly; a case of FPC with complete Gardner's syndrome. The latter patient (T83, III-5) was a male aged 41 years who had very characteristic features represented by 29 epithelial cysts up to the size of a pigeon's egg on the face and other parts of body surface, 3 large fibrous tumours in the neck and bottom and a osteoma of 2·7 cm in diameter around the left mandibular joint detected on a craniogram. Examination of his daughter, who was aged 10 years, revealed a lump on her head but rectal

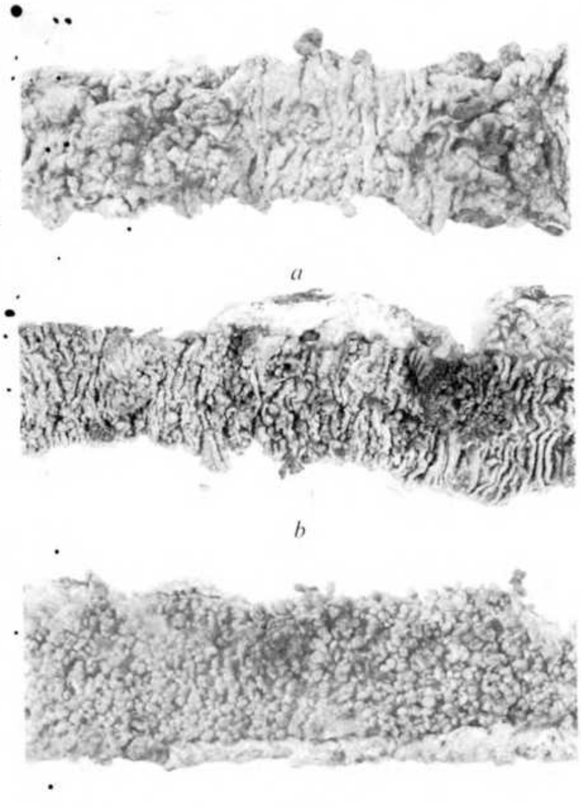


Fig. 2. Typical appearances of extensive diffuse adenomatosis in the resected colons of 3 polypotic members of family T78: a male of 56 years, T78 II-f6 (*a*) and his two daughters, T78 III-1 (*b*) and T78 III-4 (*c*).

examination was refused. The details of this family have been described by Ohtsuka (1973).

In none of these cases were lumps palpated around the jaw.

Dental findings

Characteristic radio-opaque lesions were detected in the maxillary and mandibular bone on panoramic X-rays in 27 out of 29 cases with FPC (93·2 per cent). In only 3 out of the 19 members of FPC families who were free of polyposis were such findings detected. The cases with polyposis of other types showed negative results.

The features of the lesions in question were most clearly demonstrated on panoramic X-rays (*Fig.* 3) compared with other radiological views.

The lesions have the following characteristics. They are localized and have increased radio-opacity with rather sharp borders; their size varies from 3 to 10 mm in diameter, and they are mostly round but sometimes with irregular margins; the degree of radio-opacity differs between lesions and within a lesion. The density is usually equivalent to that of bone cortex.

While they always appeared in the mandible, lesions in the maxilla were detected in 2 cases. In the mandible they were located mostly in the teeth-bearing part and never in the ramus. Many were found near the dental apex but never fused with it, while some were entirely separate from it.

The lesions were solitary in 7 cases and multiple, with up to 14 foci, in 19 cases. There was no observed significant relationship between the number of radio-opacities and the manifested associated lesions as shown in *Table I*. This is illustrated by the fact that the polypotic members of T78 family who were classified as simple FPC demonstrated most remarkable findings on panoramic X-rays (*Fig.* 3).

The lesions detected in the patients without polyposis were always solitary and very small.

The film of the case with complete Gardner's syndrome showed various lesions, including a small radio-opacity similar to those mentioned above, two composite odontomas, a large osteoma around the mandibular joint and many impacted teeth (*Fig.* 4). His daughter also showed a small radio-opacity in her mandible.

Another noticeable finding of the FPC patients was the frequent appearance of impacted teeth (in 11 cases or 35·7 per cent).

Discussion

Localized radio-opacities on X-rays of the mandibular and maxillary regions have been known as non-specific findings. The incidence of these in a normal population, however, may be rather low; focal radio-opacities of any type were detected on 26 (5·9 per cent) out of 438 panoramic X-ray films taken at the Department of Dental Radiology, Tokyo Medical and Dental University, in 1972; Boyne (1960) detected localized radio-opacities in only 1·4 per cent of full mouth X-rays of male patients at a dental clinic.

These data suggested that the incidence of radio-opacities of 93 per cent in cases with FPC was unusual. The fact that such radio-opacities were not detected in patients with other polyposis indicated that the condition is particularly associated with FPC.

Furthermore, our findings were considered to be different from simple condensing or sclerosing osteitis which accounts for most of the radio-opaque lesions seen on X-rays of the jaws on routine dental examination. The latter radio-opacities are usually solitary and occur around the dental apex in the premolar or molar region; contrary to this, our lesions were mostly multiple and also appeared in the incisor region. In addition the increased radio-opacity and the rather sharp margins indicate that they are more like osteomas than sclerotic lesions. Since no swelling around the jaw or in the oral cavity was detected clinically, lesions such as exostosis, torus or periosteal osteoma may be excluded. The lesions detected are therefore thought to correspond to central osteoma or endosteoma and the name 'occult osteomatous lesion' is proposed.

Biopsies of the lesions have not been carried out, first, because of the impossibility of obtaining sufficient material from such small lesions deeply hidden in the mandibular bone without extensive

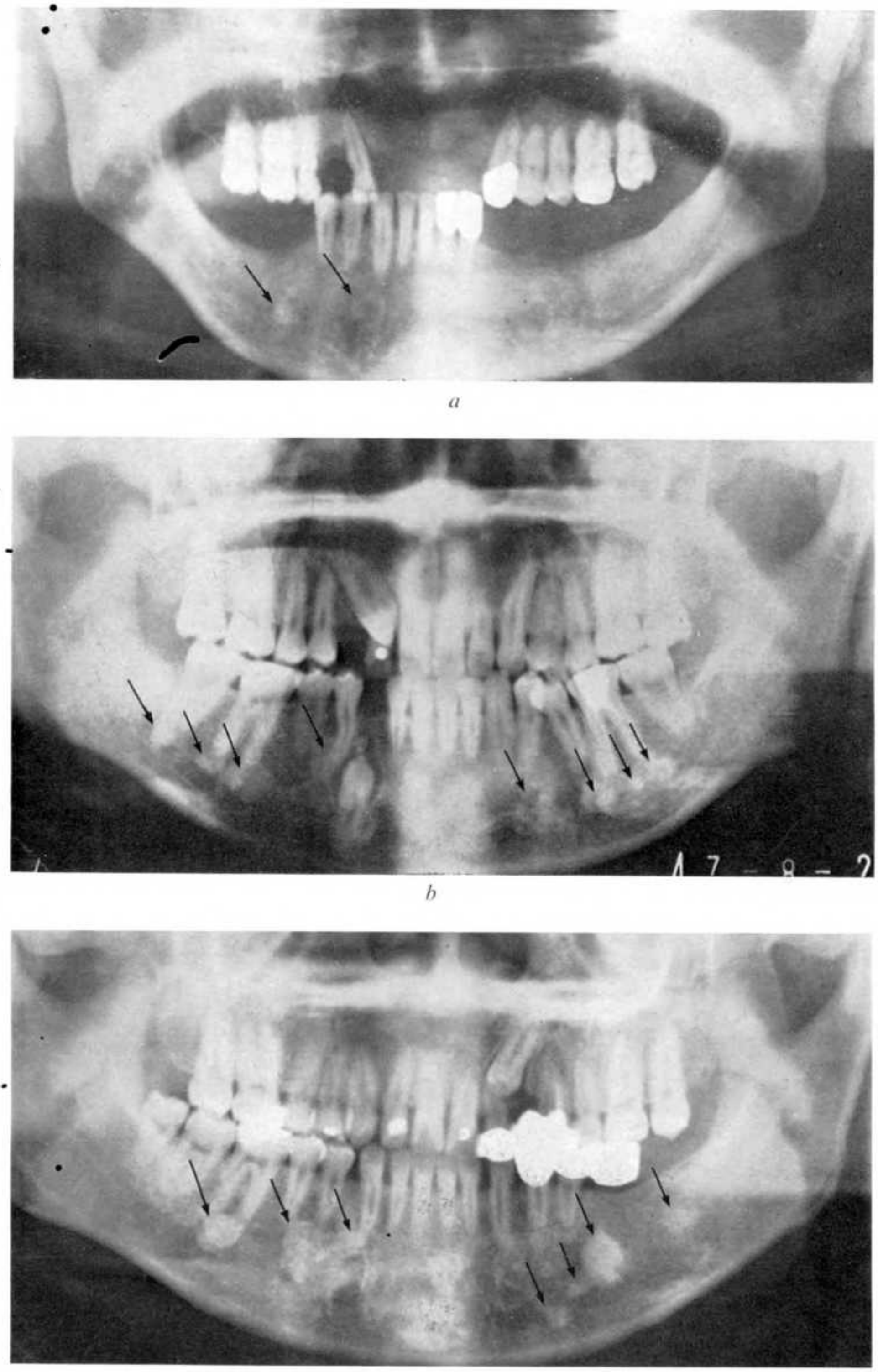


Fig. 3. Panoramic X-rays of the three polypotic members of family T78 shown in *Fig. 2*. *a*, Film of T78 II-f6 showing two round opacities with a rather sharp border located apart from the apex of the teeth in the right body of the mandible. *b*, Film of T78 -III-1 showing multiple (about eleven) opacities distributed in the body of the mandible, and an impacted canine. *c*, Film of T78 III-4 showing at least six radio-opaque foci. One of them located in the left premolar region is particularly large, 2 cm in diameter, and has quite a sharp border. The upper left canine is impacted.

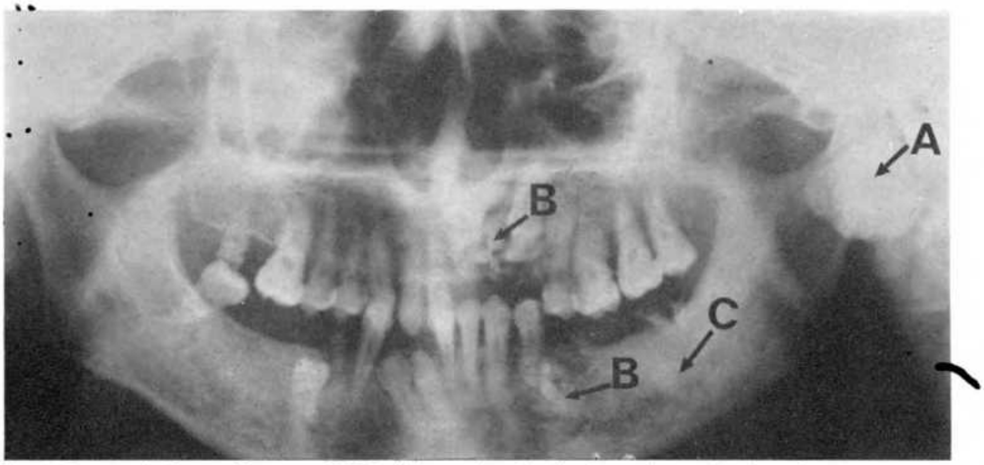


Fig. 4. Panoramic X-ray of a case of FPC with complete Gardner's syndrome showing a large osteoma (A), two composite odontomas (B), a focal radio-opaque lesion (C) and many impacted teeth.

damage to an unsymptomatic part of the patients, and secondly, because histological examination of a biopsy specimen, if it should be obtained, could not provide any more conclusive information than that provided by the radiological examination.

Although the explanation of the pathogenesis of the lesions will not be known until a large block of mandibular bone can be examined at necropsy of polypotic patients we believe that our findings are significant.

There is still dispute over the location of Gardner's syndrome in the classification of polyposis. McKusick (1962) considered that Gardner's syndrome belongs to a genetically isolated category from simple FPC, while Smith (1958, 1968) believed that the difference was merely a matter of expression of the associated traits of essentially the same disease with a single aetiology.

By comparing the essential characteristics, other than the associated stigmata, of the two diseases no significant differences were found by Utsunomiya et al. (1972).

In addition to this evidence, the present finding that in most of the cases with FPC, regardless of the association of Gardner's stigmata, osteomatous changes were detected in the mandible, which is the most common site of manifested osteoma in cases described as typical 'Gardner's syndrome', suggests that Gardner's syndrome and simple FPC should not be considered as different aetiological categories, and indicates that FPC has the potential to produce a variety of neoplastic lesions other than the colonic lesion. Utsunomiya et al. (1974) showed the very frequent association of adenomatosis of the stomach, and the occurrence of many other kinds of neoplastic lesion in this disease is known (Smith, 1958, 1968; McAdam and Goligher, 1970).

The frequent occurrence of osseous lesions, particularly in the mandible, in FPC in relation to the presence of impacted teeth in these patients might form the basis of another study.

In practice, the occult osteomatous changes described in this paper are considered to present a useful finding for the early detection of the polyposis carrier in the FPC family. In fact, we now perform routine panoramic X-rays of the jaws of members of a polypotic family and in many instances have predicted the presence of polyposis before rectal examination.

References

BARTHOLOMEW L. G., DAHLIN D. C. and WAUGH J. M. (1957) Intestinal polyposis associated with mucocutaneous melanin pigmentation (Peutz–Jeghers syndrome). *Gastroenterology* **30**, 434–451.

BOYNE P. J. (1960) Incidence of osteosclerotic areas in the mandible and maxilla, *J. Oral Surg.* **18**, 486–491.

CHANG C. H., PIATT E. D., THOMAS K. E. and WANTE A. L. (1968) Bone abnormalities in Gardner's syndrome. *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **103**, 645–652.

FADER M., KLINE S. N., SPATZ S. S. and ZŪBROW H. J. (1962) Gardner's syndrome and a new dental discovery. *Oral Surg.* **15**, 153–172.

GARDNER E. J. and PLENK H. P. (1951) Hereditary patterns for multiple osteomas in a family group. *Am. J. Hum. Genet.* **4**, 31–36.

GARDNER E. J. and RICHARDS R. C. (1953) Multiple cutaneous and subcutaneous lesions occurring simultaneously with hereditary polyposis and osteomatosis. *Am. J. Hum. Genet.* **5**, 139–148.

JEGHERS H., MCKUSICK V. A. and KATZ K. H. (1949) Generalized intestinal polyposis and melanine spots of the oral mucosa, lips and digits: a syndrome of diagnostic significance. *New Engl. J. Med.* **241**, 933–1005, 1031–1036.

MCADAM W. A. F. and GOLIGHER J. C. (1970) The occurrence of desmoids in patients with familial polyposis coli. *Br. J. Surg.* **57**, 618–631.

MCKUSICK V. A. (1962) Genetic factors in intestinal polyposis. *JAMA* **182**, 271–277.

OHTSUKA A. (1973) A case of Gardner's syndrome. *Jap. J. Plast. Reconstr. Surg.* **16**, 240–250.

ROSS P. (1966) Gardner's syndrome. *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **96**, 298–301.

SMITH W. G. (1958) Multiple polyposis: Gardner's syndrome, and desmoid tumours. *Dis. Colon Rectum* **1**, 323–332.

SMITH W. G. (1968) Familial multiple polyposis: research tool for investigating the etiology of carcinoma of the colon? *Dis. Colon Rectum* **11**, 17–31.

THOMAS K. E., WATNE A. L., JOHNSON J. G., ROTH E. and ZIMMERMANN B. (1968) Natural history of Gardner's syndrome. *Am. J. Surg.* **115**, 218–226.

UTSUNOMIYA J. (1973) The present status of familial polyposis of the colon. In: NAKAHARA W. (ed.) *Proceedings of the Third International Symposium of the Princess Takamatsu Cancer Research Fund, Analytical and Experimental Epidemiology of Cancer*. University of Tokyo Press, pp. 339–340.

UTSUNOMIYA J., MAKI T., HAMAGUCHI E. and AOKI N. (1974) Gastric lesion of familial polyposis of the large intestine. *Cancer* **74**, 745–754.

UTSUNOMIYA J., SUZUKI H., HAIBARA H. and IWAMA T. (1972) Gardner's syndrome. (In Japanese.) *J. Clin. Cancer* **18**, 79–100.

VEALE A. M. O., MCCOLL I., BUSSEY J. H. R. and MORSON B. C. (1966) Juvenile polyposis coli. *J. Med. Genet.* **3**, 5–16.

Br. J. Surg. Vol. 62 (1975) 52–56

The continent ileostomy of Kock (ileal intra-abdominal reservoir)

Experience with 9 cases operated on for ulcerative colitis

JAN F. HALVORSEN AND PETER HEIMANN*

SUMMARY

A series of 9 patients with ulcerative colitis undergoing proctocolectomy and ileal intra-abdominal reservoir is reported. Eight patients are continent and 1 is incontinent. Early and late postoperative complications, work capacity and social and sexual functions are described.

PATIENTS with conventional ileostomies after proctocolectomy are generally held to adapt well to their situation (Biermann et al., 1966; Watts et al., 1966b; Goligher et al., 1968; Roy et al., 1970; Scott et al., 1970). After a long and disabling illness—in most cases ulcerative colitis—there is a marked improvement in the general physical condition of the patient, and the existence of an ileostomy may seem a reasonable price to pay for better health. The majority of patients return to their full pre-disease work capacity and their social activities are not mentionably restricted (Watts et al., 1966b; Goligher et al., 1968; Roy et al., 1970; Scott et al., 1970). If questioned closely, however, a significant number of patients with an ileostomy admit that they have problems. There are many drawbacks of even a well-functioning ileostomy: the flow of intestinal contents is more or less continuous in a quantity of about 600 ml/24 hours (Goligher et al., 1968), is not voluntarily controlled and necessitates the continual wearing of external bags. Even with modern appliances there is always the possibility of leakage and unpleasant odour (DiZerega et al., 1967). Skin irritation and maceration from the effluent or the bag glue are the most frequent complications and occur in 24–70 per cent of patients (Biermann et al., 1966; Watts et al., 1966b; DiZerega et al., 1967; Roy et al., 1970). The wearing of bulky external appliances also puts some restraint on the social lives of the patients, especially during the bathing season and during periods of fashionable body exposure. Some patients find that care of the ileostomy and the appliances requires too much time (Roy et al., 1970). Sexual dysfunction occurs in 25–30 per cent of cases (Watts et al., 1966b; Roy et al., 1970), and probably is due to the combined effect of the rectal excision and the presence of an artificial anus. A small number of patients simply cannot adjust to a life with an ileostomy and feel miserable and crippled (Watts et al., 1966b; Roy et al., 1970).

These problems prompted Kock (1969, 1971, 1973) to create an ileal intra-abdominal reservoir that gave patients the possibility of having voluntary control of emptying, and made the wearing of bags unnecessary. In a recent publication (Kock, 1973) he reported the results in a series of 90 patients. Other authors (Akovbiantz and Kock, 1972; Beahrs and Adson, 1973; Cameron, 1973; Halter, 1973; Schaudig et al., 1973; Beahrs et al., 1974) have published smaller series. The present paper reports the results in 9 patients with ulcerative colitis treated with proctocolectomy and ileal intra-abdominal reservoir.

Materials and methods

Nine patients (6 men and 3 women) with ulcerative colitis, 7 with total and 2 with near total involvement of the colon, underwent proctocolectomy with the creation of an ileal intra-abdominal reservoir. These patients were followed up during the period from December 1971 to April 1974 (observation time 2–28 months). The age distribution of the patients was 16–56 years, and the duration of the colitis ranged from 9 months to 15 years. Six patients were operated on electively and 3 during an acute attack. In 8 patients the operation was done as a one-stage procedure and in 1 patient as a two-stage procedure.

The construction of the reservoir was performed as shown in *Fig.* 1. The terminal 15 cm of the distal ileum were left untouched, and the 30 cm of ileum proximal to this were folded and sutured together along the antimesenteric border with a continuous 3/0 Dexon suture. The legs of the U were then opened, the incision being made 3 cm longer in the proximal leg in order to separate the outlet from the inlet. The mucosa was sutured with a continuous 3/0 Dexon suture. The terminal ileum was then partly intussuscepted into the reservoir, making a 4-cm long nipple, this being fixed with eight to ten 2/0 silk sutures through the intestinal wall with the ileostomy tube in place. The intestinal plate formed by the opened ileum was then folded and closed in two layers with 3/0 Dexon. The reservoir was manipulated into shape by putting it in between the mesenteric leaves. The patency of the reservoir and the valve was tested by injecting air into it through a catheter while clamping the afferent limb. Removal of the catheter should not result in leakage of air through the outlet. The air was removed by reinserting the catheter. The ileostomy opening in the skin was made at a site lower down than is usual for a conventional ileostomy, so as to be

---

* Department of General Surgery, University Clinic, Bergen, Norway.

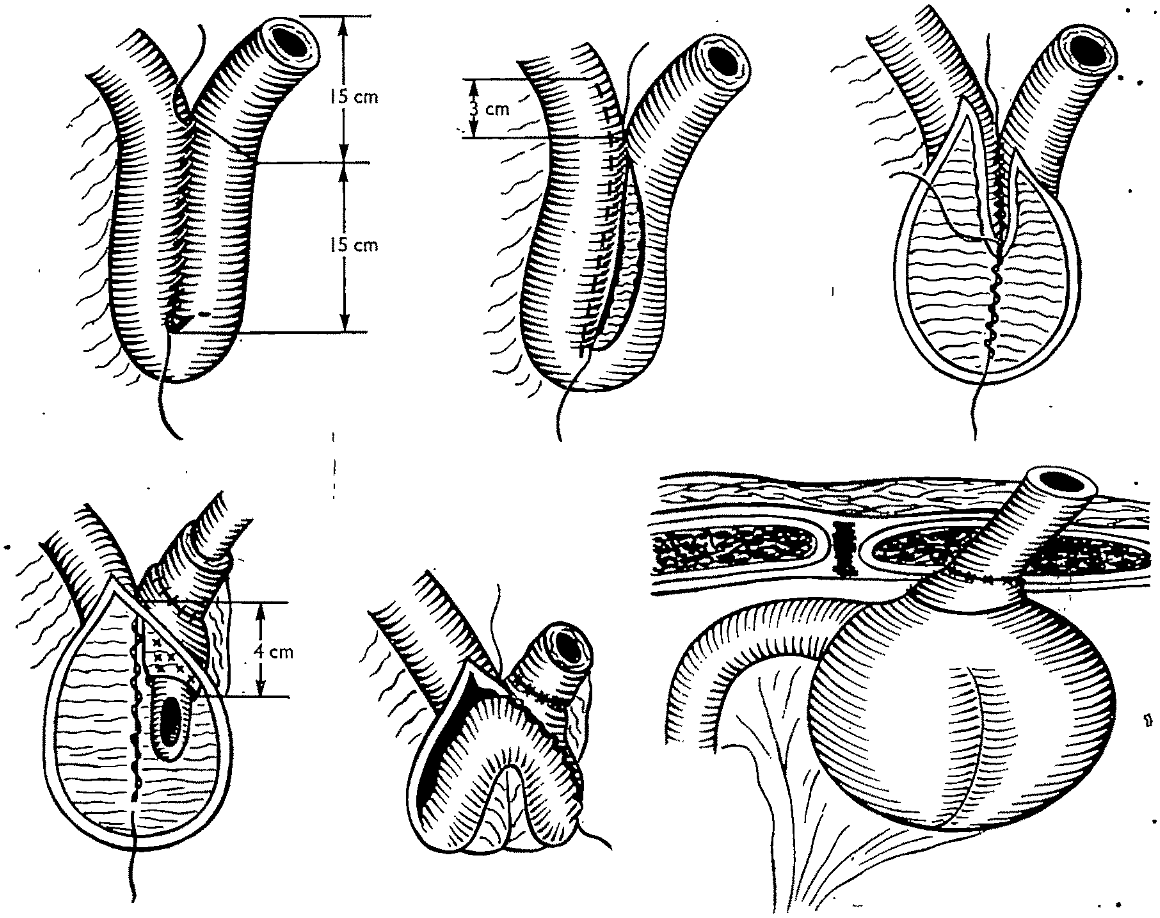


Fig. 1. Diagrammatic representation of the operative procedure.

situated well below the waistline. From this skin opening a tunnel was made slightly obliquely through the rectus muscle, and the terminal segment of the ileum pulled through the channel. The reservoir was fixed to the anterior abdominal wall with interrupted silk sutures and the space lateral to the reservoir closed by suturing the edge of the mesentery to the parietal peritoneum. Excess ileum was resected and a flat ileostomy made by suturing the skin to the cut edge of the intestine with interrupted 2/0 chromic catgut sutures. The ileostomy tube was left in place to drain the reservoir for the first 7 postoperative days through a wide bore tube into a plastic bag. On the eighth day the ileostomy tube was removed and then reintroduced at 3-hourly intervals. It was still left *in situ* at night for another 3–4 days, after which time emptying of the reservoir was performed at increasing intervals until after 3–4 months' time only 3–5 emptyings a day were necessary. The stoma was covered by a small bandage between emptyings.

Five reservoirs were originally made according to Kock's procedure B without a nipple and 4 according to procedure C with a nipple (Kock, 1973). Three patients who originally had no nipple have been reoperated on with the construction of a nipple because of incontinence after the first operation. At present therefore 7 reservoirs have a nipple. *Table I* lists age and sex, duration of the disease, duration of and discontinuance of steroid treatment in relation to the operation and degree of involvement of disease.

Results

There was no mortality. All the patients are alive and have been followed up. *Table II* lists the early and late postoperative complications.

Early complications

In 2 cases there was troublesome bleeding from the pelvic cavity during the operation. One was managed by tamponade from below and removal of the pack the next day, and the other underwent reoperation on the third day to ensure haemostasis. One patient had a reoperation on the seventh postoperative day for intestinal obstruction caused by adhesions. Three patients developed a fistula from the reservoir to the abdominal wound, but they all healed spontaneously

Table I: DETAILS OF THE PRESENT SERIES

Case no.	Sex	Age (yr)	Duration of disease	Duration of steroid therapy	Discontinuance of steroid therapy	Degree of involvement
1	M	35	9 mth	4 mth	3 mth	Total
2	M	37	15 yr	4 yr	2·5 mth	Near total
3	M	16	12 yr	3 mth	1 yr	Total
4	M	56	2 yr	2 mth	After operation	Total
5	M	31	5 yr	9 mth	After operation	Near total
6	F	29	13 yr	1 mth	6 yr	Total
7	F	47	4 yr	2 mth	4 mth	Total
8	M	25	3 yr	1 yr	After operation	Total
9	F	34	6 yr	2 mth	2 mth	Total

Table II: POSTOPERATIVE COMPLICATIONS

Postoperative complications	No. of cases
Early	
Haemorrhage from the pelvic cavity	2
Intestinal obstruction (adhesions)	1
Fistula from reservoir to abdominal wound	3
Transient hepatic insufficiency (cirrhosis)	1
Late	
Partial disinvagination of the nipple	3
Perineal sinus (silk sutures)	1
Pulmonary embolus	1

in the course of 1–2 weeks with the ileostomy tube left in place. Two of these patients were operated on during an acute attack of ulcerative colitis and 1 following 2 months of continuous steroid therapy. One patient, who prior to the operation had cirrhosis of the liver, developed transient hepatic insufficiency with a moderate jaundice that disappeared after 2 weeks.

Late complications

The main late complication has been difficulties in introducing the tube into the reservoir. This occurred in 3 patients in whom a nipple had been constructed. X-ray studies with the injection of contrast through the stoma demonstrated lengthening of the efferent limb due to partial disinvagination of the nipple. Since the nipples were to some extent still intact, the simplest operation of shortening the efferent limb was performed. All of them are now continent, though occasionally the patients wear a bag for safety. One patient developed a perineal sinus that persisted for 1 year from which silk sutures repeatedly were removed and which has now healed. One patient suffered a pulmonary embolus 2 months after the operation and was successfully treated with Streptokinase and Marevan.

Continence

Table III lists the results as regards continence. Four patients are continent for gas and fluid, empty their reservoirs about five times daily and never wear bags. Four patients are continent, but occasionally wear a bag for safety in certain situations. One patient is incontinent and always wears a bag.

Sexual function

One male patient is impotent and 1 female has dyspareunia.

Table III: CONTINENCE AFTER OPERATION

Result	With nipple	Without nipple
Continent	6	2
Incontinent	1	0

Social function

The incontinent patient feels somewhat restricted socially.

Work capacity

Eight patients have returned to full pre-disease work capacity. One recently operated patient has not yet returned to work.

Discussion

The incidence of postoperative complications in this small series is about the same as that of other published series of ulcerative colitis treated with proctocolectomy and conventional ileostomy (Watts et al., 1966a, b; Roy et al., 1970; Scott et al., 1970). Three patients developed a transient fistula from the reservoir to the abdominal wound. Two of them were operated on during an acute attack and 1 following 2 months of continuous steroid therapy. It is generally accepted that these factors predispose to delayed healing and anastomotic leakage (Watts et al., 1966a; Scott et al., 1970; Kock, 1973). In 3 cases partial disinvagination of the nipple occurred, causing lengthening of the efferent limb and difficulties in introducing the tube. They were all treated by shortening the efferent limb, and though they are still continent and experience no difficulties in inserting the tube, the correct operation would probably have been re-laparotomy and reconstruction of the nipple. We did not scarify the serosal surface when making the nipple in these 3 patients, as has since been recommended by Kock (1973). It seems that the presence of the ileal intra-abdominal reservoir did not seriously jeopardize the postoperative course in our series.

In 1 case a persistent perineal sinus developed from which silk sutures were removed repeatedly by curettage. The sinus healed after 1 year. This patient was operated on during an acute attack of ulcerative colitis after 9 months of continuous steroid treatment. Although it is believed that the sinus was caused by a foreign body reaction to silk, these factors may have contributed to its development and persistence. Watts et al. (1966b) found that the incidence of perineal sinus increased fourfold if steroids were administered for more than 6 months prior to surgery.

Eight patients have returned to their work and have regained full pre-colitis work capacity. One patient who has recently been operated on is still incapacitated.

The patient with the perineal sinus also developed migrating arthritic symptoms in the joints of the upper extremities. These symptoms first appeared after the operation, but there were no objective signs of joint disease. Watts et al. (1966b) reported persistent arthritic symptoms in 5 out of 131 patients treated surgically for ulcerative colitis. They concluded, however, that the symptoms were not due to true colitic arthritis.

A 56-year-old man has become impotent and a 47-year-old woman has developed dyspareunia after the operation. This is a not uncommon experience after rectal excision (Watts et al., 1966b). The incidence of postoperative sexual dysfunction increases with advancing age (Watts et al., 1966b; Roy et al., 1970), and may well be a reflection of the physical and psychological effects of a major operation with the creation of an artificial anus in individuals whose sexual function is already waning. The other patients have not reported any change in their sexual habits, though 2 young unmarried males express a certain anxiety as to the reaction of the opposite sex when their affliction is discovered.

Originally 5 reservoirs were made without a nipple. Three of these have later been fitted with a nipple because of incontinence. At present 7 reservoirs have a nipple. Eight patients are continent for gas and fluid and empty their reservoirs three to five times daily, but 4 of them occasionally wear a bag for safety, though most of the time they cover the stoma with a bandage. One patient who originally had a nipple is incontinent, probably owing to disinvagination of the nipple. This, however, has not been verified because he does not wish further examination and treatment. Thus 6 out of the 7 reservoirs with a nipple and both the remaining reservoirs without a nipple are continent. It seems that the nipple practically ensures continence.

The patient who was operated on in two stages originally had a conventional ileostomy that was converted to an ileal intra-abdominal reservoir because of skin maceration. He is now continent, and his skin is normal.

The 8 continent patients are very satisfied with their stomas, and lead normal or near normal lives both professionally and socially. The incontinent patient feels restricted socially and is also impotent.

We have not performed absorption studies in our patients, but none of them has hitherto shown any clinical signs of deficiencies. Jagenburg et al. (1971) studied the absorption of D-xylose, fat and L-phenylalanine in 10 patients with a conventional ileostomy and in 10 patients with an ileal intra-abdominal reservoir, and found no differences in the two groups. The bacterial flora of the reservoir is intermediate between the flora of the effluent from a conventional ileostomy and that of normal faeces (Branberg et al., 1972). Morphologically there is flattening of the villi with an intact brush border, a finding that may indicate an adaption to the change in the microbial population (Kock, 1973). There is, however, no change in the disaccharidase activity (Kock et al., 1972).

According to our experience with 9 patients the continent ileostomy of Kock is a valuable alternative to the conventional ileostomy. It is also recommended in patients who for some reason are unhappy with their conventional ileostomy, especially those with skin problems. The reservoir should be made as an elective procedure, and in acute situations a conventional ileostomy is preferred. This may easily be changed into an ileal intra-abdominal reservoir at a later date. A reservoir should not be made in cases of Crohn's disease of the colon, because a recurrence in the reservoir will necessitate the removal of too much ileum (Kock, 1973). In our experience the following technical details seem important. The efferent limb should be short and brought out slightly obliquely through the rectus muscle. When constructing the nipple the serosal surface should be coagulated with diathermy and the fixing sutures of the nipple should be silk to prevent disinvagination of the nipple. Difficulties in introducing the tube may indicate that disinvagination has occurred. If verified by stomography and endoscopy the correct treatment of this complication is re-laparotomy and reconstruction of the nipple.

References

AKOVBIANTZ A. and KOCK N. (1972) Die kontinente Ileostomie. *Helv. Chir. Acta* **39**, 259–262.

BEAHRS O. H. and ADSON M. A. (1973) Ileal pouch with ileostomy rather than ileostomy alone. *Am. J. Surg.* **125**, 154–158.

BEAHRS O. H., KELLY K. A., ADSON M. A. and CHONG G. C. (1974) Ileostomy with ileal reservoir rather than ileostomy alone. *Ann. Surg.* **179**, 634–638.

BIERMANN H. J., TOCKER A. M. and TOCKER L. R. (1966) Statistical survey of problems in patients with colostomy or ileostomy. *Am. J. Surg.* **112**, 647–650.

BRANBERG Å., KOCK N. G. and PHILIPSON B. (1972) Bacterial flora in intraabdominal ileostomy reservoir. A study of 23 patients provided with "continent ileostomy". *Gastroenterology* **63**, 413–416.

CAMERON A. (1973) The continent ileostomy. *Br. J. Surg.* **60**, 785–790.

DIZEREGA D., BUCKNER F. A., TOCKER A. M., BIERMANN H. J. and TOCKER L. R. (1967) Ileostomy problems. The patients' viewpoint. *J. Kans. Med. Soc.* **68**, 40–44.

GOLIGHER J. C., DE DOMBAL F. T., WATTS J. M. and WATKINSON G. (1968) *Ulcerative Colitis.* London; Baillière, Tindall & Cassell.

HALTER F. (1973) Die Betreuung des Patienten mit Ileostomie. Schweiz. Med. Wochenschr. **103**, 168–171.

JAGENBURG R., DOTEVALL G., KEWENTER J., KOCK N. G. and PHILIPSON B. (1971) Absorption studies in patients with "intraabdominal ileostomy reservoirs" and in patients with conventional ileostomies. *Gut* **12**, 437–441.

KOCK N. G. (1969) Intraabdominal "reservoir" in patients with permanent ileostomy. Preliminary observations on a procedure resulting in fecal "continence" in five ileostomy patients. *Arch. Surg.* **99**, 223–231.

KOCK N. G. (1971) Ileostomy without external appliances: a survey of 25 patients provided with intra-abdominal intestinal reservoir. *Ann. Surg.* **173**, 545–550.

KOCK N. G. (1973) Continent ileostomy. *Progr. Surg.* **12**, 180–201.

KOCK N. G., ASP N.-G., DAHLQVIST A. and PHILIPSON B. (1972) Disaccaridase activity in the terminal ileum of patients with intraabdominal ileostomy reservoir. *Scand. J. Gastroenterol.* (*Suppl.*) **16**, 36.

ROY P. H., SAUER W. G., BEAHRS O. H. and FARROW G. M. (1970) Experience with ileostomies. Evaluation of long-term rehabilitation in 497 patients. *Am. J. Surg.* **119**, 77–86.

SCHAUDIG A., KOCK N., V. BARY S. and NAKANO H. (1973) Die kontinente Ileostomie nach Kock. *Munch. Med. Wochenschr.* **115**, 290–295.

SCOTT H. W. jun., WIMBERLY J. E., SHULL H. J. and LAW D. H. (1970) Single stage proctocolectomy for severe ulcerative colitis. Comparison with less extensive surgical procedures. *Am. J. Surg.* **119**, 87–94.

WATTS J. M., DE DOMBAL F. T. and GOLIGHER J. C. (1966a) Early results of surgery for ulcerative colitis. *Br. J. Surg.* **53**, 1005–1014.

WATTS J. M., DE DOMBAL F. T. and GOLIGHER J. C. (1966b) Long-term complications and prognosis following major surgery for ulcerative colitis. *Br. J. Surg.* **53**, 1014–1023.

Br. J. Surg. Vol. 62 (1975) 57–58

Torsion of the testis: a review of 22 cases

Improved diagnosis and earlier correction

M. G. GREANEY*

SUMMARY

Greater awareness of the possibility of torsion of the testis and earlier exploration has led to the saving of 14 out of 19 acutely twisted testicles.

PREVIOUS reports have shown that up to 62 per cent of patients presenting with torsion of the testis have required orchidectomy. Delays in diagnosis and exploration are said to account for this high figure (Barker and Raper, 1964; Allan and Brown, 1966). This paper reviews all the cases of torsion admitted to two surgical units at the Royal Infirmary, Sheffield, during the years 1963–73, when there was greater awareness of this condition.

Materials and methods

Twenty-two cases with the final index diagnosis of torsion of the testis were reviewed. All presented as acute surgical emergencies, except for 3 patients. These 3 cases presented as outpatients with recurrent testicular pain. In 2 the pain was in the right testis of 4 months' and 5 years' duration respectively, the latter patient having previously had an undescended left testis removed at herniotomy. In the third there was recurrent left testicular pain.

All the cases were explored, and the diagnosis of torsion confirmed at operation.

In every case the affected testis was in the scrotum, and torsion was of the intravaginal type. The anatomical anomalies, which are bilateral in torsion of the testis, have previously been described (Clarke, 1956; Angell, 1963; Barker and Raper, 1964). Clinically, the abnormalities are seen in the standing patient as bilateral horizontally lying testes.

Incidence

This series does not include children under 13 as they are not admitted to this hospital. Although the maximum incidence is described as being in the late teens it should be noted that 54 per cent of this series were older, indeed one patient was 63 years old, and it would appear that torsion of the testis can occur at any age (*Table I*).

Clinical features

Classic descriptions of acute torsion of the testis remark on the sudden onset of pain in the groin, sometimes associated with vomiting, and the finding of a swollen and acutely tender affected testis, with oedema and erythema of the overlying scrotum. The clinical features of the 19 patients presenting acutely are shown in *Table II*. This shows that the most important clinical signs are: (1) a tender swollen testis; (2) the horizontal lie of either the affected or the opposite testis; (3) the absence of urinary symptoms. Only one patient had dysuria but since he had a positive urine culture he may have had a concomitant urinary infection.

It should be noted that: (*a*) pyrexia is non-specific; (*b*) although the onset of pain is rapid in contrast to epididymitis it is not normally sufficiently sudden to be noted as such; (*c*) the condition is found equally on either side.

Table I: AGE DISTRIBUTION

Age (yr)	No. of cases
13–20	11
21–30	8
31+	3

Table II: CLINICAL FEATURES IN 19 CASES PRESENTING ACUTELY

Clinical feature	No. of cases	%
Pain		
Sudden onset	1	5
Scrotal	17	90
Confined to abdomen initially	2	11
Subsequent radiation to groin/lower abdomen	6	32
Nausea and vomiting	3	16
Tender, swollen testis	19	100
Horizontal lie of affected testis	7	37
Horizontal lie of contralateral testis	8	42
Dysuria	1	5
Temperature noted in admission notes in 8 cases		
Normal	3	
36·4–37·8 °C	5	
Urine samples in 6 patients		
No cells on microscopy	4	
Many WBC/high power field	1	
Single WBC/high power field	1	
Organisms cultured but no WBC	1	
Side affected in total number of patients (22)		
Right	10	
Left	12	

Recurrent torsion

Of the 22 patients (including the 3 presenting non-acutely), 15 gave a history of similar episodes of previous testicular pain. All were of short duration, no more than 3 hours, and had occurred, on occasions, over a maximum period of 2 years. Seven of the 15 complained of a single episode of pain, the earliest being 5 years previously and at that time this patient had fixation of the affected testis.

---

* Royal United Hospital, Bath.

Table III: DURATION OF SYMPTOMS PRIOR TO ADMISSION AND SUBSEQUENT TREATMENT

Duration of symptoms (hr)	Orchidopexy	Orchidectomy
0–6	11	
7–12	1	1
13–48	—	—
48+	2	2
Duration unknown	2	
Non-acute	3	

Treatment

As previously mentioned, all the cases were surgically explored using scrotal incisions, the diagnosis confirmed and the necessary operative treatment instituted. Treatment was fixation (orchidopexy) of the affected testis if considered viable after untwisting the spermatic cord. The testicle was fixed to the spermatic cord with interrupted thread sutures to maintain an upright position. The tunica vaginalis was then usually everted and the scrotum closed with catgut to the dartos and clips to skin. If the testis appeared gangrenous and remained so after allowing time for improvement of the circulation orchidectomy was performed. In one case viability was doubtful and orchidopexy was later complicated by a scrotal abscess.

The unaffected testis requires fixation at the time of operation to prevent subsequent torsion and this was performed in 19 of the 22 cases.

Barker and Raper (1964) emphasized the importance of early operation and subsequent outcome and *Table III* shows the necessary management in relation to the duration of symptoms before admission to hospital.

In 3 of the cases the postoperative course was complicated by local inflammation. In 2 there was scrotal abscess formation, one of these patients being found to have many white cells in the urine in a sample taken preoperatively. In the other patient a stitch abscess developed.

Follow-up

At the time of discharge from the outpatients' clinic 17 of the 19 salvaged testicles were reported as normal. Both of the abnormal testes were in patients who had suffered from postoperative scrotal infection in whom the affected testis was then atrophic. Seven of the 19 responded to a recent request to come for re-examination. Only one had evidence of serious damage to the affected testis and he had been one of the patients in whom a scrotal abscess had complicated the postoperative course.

Discussion

Torsion of the testis unless quickly diagnosed and treated leads to loss of the testis. In this series of 22 cases in only 4 was the testis definitely lost and in another the testis probably atrophied. In 3 orchidectomy was performed and in the other 2 there was postoperative scrotal abscess formation. This compares favourably with results in earlier papers: Angell (1963), 4 orchidectomies in 14 patients; Barker and Raper (1964), 18 in 38 patients; Allan and Brown (1966), 36 in 58 patients; Chapman and Walton (1972), 32 in 67 patients.

The results of our series would seem to show a greater awareness of the condition at the present time and of the necessity for early diagnosis and operation. In all cases in which there is doubt over the diagnosis of an acutely tender, swollen testis, especially one noticed to be in a horizontal position with the patient standing and with the contralateral testis in a similar position, exploration should be carried out.

Acknowledgements

I am grateful to Mr D. H. Randall and Mr C. Jones for allowing me to review these patients who have been under their care.

References

ALLAN W. R. and BROWN R. B. (1966) Torsion of the testis: a review of 58 cases. *Br. Med. J.* **1**, 1396.

ANGELL J. C. (1963) Torsion of the testicle, a plea for diagnosis. *Lancet* **1**, 19.

BARKER K. K. and RAPER F. P. (1964) Torsion of the testis. *Br. J. Urol.* **36**, 35–41.

CHAPMAN R. M. and WALTON A. J. (1972) Torsion of the testis and its appendages. *Br. Med. J.* **1**, 164.

CLARKE S. (1956) Letter to the Editor. *Lancet* **2**, 842.

Br. J. Surg. Vol. 62 (1975) 59–63

Surgical sterilization by vasectomy and its effect on the structure and function of the testis in man

A. S. GUPTA, L. K. KOTHARI, A. DHRUVA AND R. BAPNA*

SUMMARY

The early and late effects of vasectomy have been investigated in 40 men. Besides histopathological examination, the volume of the testis and its total content of testosterone-secreting Leydig cells have been measured.

The volume of the testis showed a wide normal variation (5·3–23·3 ml) but was not significantly changed by vasectomy. One month after vasectomy widespread degeneration of the germinal epithelium, thickening of the basement membrane and some inter-tubular fibrosis were observed. Spermatogenesis had ceased. However, cases examined 2–3½ years later showed an essentially normal structure with active spermatogenesis. This indicates that regeneration does occur spontaneously, even without recanalization. Whether the sperms formed are functionally normal remains uncertain.

The normal total Leydig cell volume was 2·2 ± 0·4 ml/testis in young adults and showed a modest increase after vasectomy, rising to 2·5 ± 0·5 ml after 1 month and 2·6 ± 0·5 ml after 2–3½ years. The findings have been discussed in the light of Steinach's (1927) original hypothesis that vasectomy can rejuvenate ageing males by improving the endocrine function of the testis.

BILATERAL vasectomy is gaining wide popularity as a contraceptive measure, particularly in developing countries such as India where it forms a major part of the population control programme. The changes that occur in the testis as a result of occlusion of its outflow tract have been repeatedly investigated in laboratory animals but the results have been variable, ranging from a marked degeneration of the seminiferous tubules and proliferation of the testosterone-secreting Leydig cells (Steinach, 1927; Houssay, 1955; Kothari et al., 1973) to practically no change at all (Harrison and Macmillan, 1954; Baillie, 1960; Smith, 1962). Besides species variation, some of the factors possibly involved are the site of seminal occlusion, interference with testicular blood supply and the accuracy of histopathological interpretation.

In view of this uncertain situation we have investigated the post-vasectomy testicular changes directly in man, paying particular attention to Steinach's (1927) original hypothesis that vas occlusion leads to a hyperplasia of the Leydig cells—the main basis for his claim that it rejuvenated ageing males.

Materials and methods

This study is based on 40 healthy fertile males between 30 and 60 years of age; these were divided into three groups:

Group A: Twenty young adults (30–35 years) undergoing vasectomy for sterilization.

Group B: Ten elderly males (50–60 years) vasectomized prior to prostatectomy (uncomplicated cases).

Group C: Ten vasectomized subjects undergoing recanalization (30–35 years).

Techniques

1. *Vasectomy*: After 1 per cent xylocaine infiltration the scrotum was incised in the midline. The vas on both sides was isolated by dissection and divided between two clamps, almost midway between the epididymis and external inguinal ring. About 1 cm of vas was totally removed and the cut ends tied firmly with silk. After attaining perfect haemostasis, the wound was closed with interrupted sutures and sealed.

2. *Open testicular biopsy*. The scrotal skin was infiltrated with 1 per cent xylocaine under proper asepsis, and a small incision was made anteriorly, midway between the upper and lower poles of the testis. The tunica vaginalis was opened. A nick in the tunica albuginea brought the testicular tissue bulging out and a piece was carefully removed by a neat cut. With gentle manipulation and a little pressure on the testis, a second biopsy piece was taken through the same cut in the albuginea. After achieving haemostasis, the wound was closed in layers and sealed. Analgesics and an anti-inflammatory drug (Tanderil, Geigy) were given if the patient complained of any pain.

The biopsy pieces were immediately fixed in Bouin's fluid. Paraffin blocks were prepared in the usual manner, using alcohol for dehydration and toluene for clearing. Sections were cut at 5 μ thickness and stained with haematoxylin and eosin.

3. *Testicular volume*: The three dimensions of the testis were first measured at their widest part along the scrotal skin using Vernier callipers. The thickness of the intervening tissues (skin surface to tunica albuginea) was then carefully measured at the site of the biopsy incision with a second pair of sterilized callipers and subtracted from the external measurements to give the true testicular dimensions. In some cases the whole testis was delivered from its tunicae and directly measured, but the previous procedure was found sufficiently accurate to make this unnecessary.

The volume of the testis was calculated by the formula, $V = \frac{4}{3}\pi r_1 r_2 r_3$, presuming the testis to be an ellipsoid such that r_1, r_2 and r_3 are its radii in the three planes (Ahmad et al., 1969).

---

* Ravindranath Tagore Medical College, Udaipur, India.

4. *Total Leydig cell volume*: This was quantitatively estimated by the histometric point-counting method. The details of the technique and its experimental verification have already been described (Kothari et al., 1972). A Leitz-type integrating eyepiece was used and, since the volume of each testis had already been determined *in situ* without any fixation or shrinkage, the total Leydig cell content could be precisely calculated in absolute terms, i.e. ml/testis.

In all cases only the left testis was investigated as being a representative of both.

Results

Testicular volume

The volume of the testis showed a large normal variation, ranging from 5·3 to 23·3 ml in the 30 males prior to vasectomy (groups A and B). The mean volume was somewhat lower in the older group of 50 years and over, compared with that in the young subjects, the values being 11·9 ± 6·5 ml and 13·6 ± 5·1 ml respectively. The difference, however, is not statistically significant.

Table I shows the testicular volume before and 1 month after vasectomy. In the older patients the volume did show a slight decrease in most instances but the change was not significant. It appears, therefore, that vasectomy does not produce any consistent change in the size of the testis which normally shows a wide variation.

Histopathology

Advancing age has been found to give rise to significant changes in the human testis (Kothari and Gupta, 1974). Thus, males above 50 years of age show scattered areas of tubular atrophy, increase in connective tissue and an appreciable proliferation of the Leydig cells. These signs of normal senility have to be kept in view while evaluating the post-vasectomy changes in testicular structure, and for the same reason they have been studied separately in the young and the old.

One month after vasectomy the testicular biopsies showed significant changes in all the 20 young adults. Marked degeneration of the germinal epithelium was evident in most of the tubules and spermatogenesis appeared to be arrested at the level of spermatocytes. A few tubules, however, still appeared normal. It was interesting to observe that the spermatogonia or basal cells withstood the degeneration and were well preserved in all the tubules.

The tunica propria which forms the limiting membrane of the seminiferous tubules showed appreciable thickening. It was now composed of several layers of wavy connective tissue lamellae and was distinctly wider than normal. A generalized increase in the intertubular connective tissue was also evident in most cases. There was, however, no evidence of increased vascularity, inflammatory reaction or necrosis.

Histologically, the interstitial or Leydig cells appeared almost unaffected by vasectomy. In some cases the collapse of the seminiferous tubules and increase in intertubular connective tissue made them more prominent, but there was no cytological evidence of active proliferation.

In males above 50 years of age the post-vasectomy changes were essentially similar but were more marked and widespread. Spermatogenesis was arrested at the spermatocyte stage in most of the tubules. The thickening of the tubular basement membrane and intertubular fibrosis, which normally accompany ageing, had been further accentuated by vasectomy. The Leydig cells stood out prominently in large clusters, and if compared with the picture in a normal (non-vasectomized) young adult would convey an impression of marked proliferation. However, we have already observed an increase in the Leydig cells as a part of the normal ageing process (Kothari and Gupta, 1974) and no further increase on account of vasectomy could be established unequivocally by histopathological examination.

Ten cases coming for recanalization 2–3½ years after vasectomy have also been included in this study since they provide an opportunity to study long term effects in young healthy adults. The need for recanalization arose because of the death or chronic illness of an only male child.

The testicular volume in these cases ranged between 8·3 and 15·1 ml with a mean of 12·2 ± 4·9 ml. This is somewhat lower than the testicular volume 1 month after vasectomy in young males (13·4 ± 4·7 ml), but the difference is not statistically significant.

Testicular biopsy revealed signs of full differentiation of germ cells and active spermatogenesis in all 10 cases. There was also clear evidence of moderate Leydig cell hyperplasia. In 4 cases, however, a vacuolating degeneration confined to a few scattered tubules was present along with some thickening of the tunica propria and intertubular fibrosis. No correlation could be established between the time lapse after vasectomy and the presence of these changes. The significant fact which emerged was the presence of active spermatogenesis in all the cases, 2–3½ years after vasectomy, along with some Leydig cell hyperplasia; scattered degeneration of a few tubules was superimposed in 40 per cent of cases. Some of these histopathological changes are shown in *Figs.* 1–5.

Total Leydig cell volume

The total Leydig cell volume has been found to be 2·2 ± 0·4 ml/testis in young healthy adults. In relative terms the Leydig cells constitute approximately 15 per cent of the testicular volume. The effect of vasectomy is shown in *Table II*.

The absolute Leydig cell content has shown a quantitative increase in all the young subjects as a result of vasectomy, but the change is modest and fails to reach a statistically significant level 1 month after vasectomy ($P > 0{\cdot}05$). However, in the recanalization cases the increase is more pronounced and statistically significant ($P < 0{\cdot}05$) compared with the normal Leydig cell content of young adults, both the groups being exactly matched for age (30–35 years). The

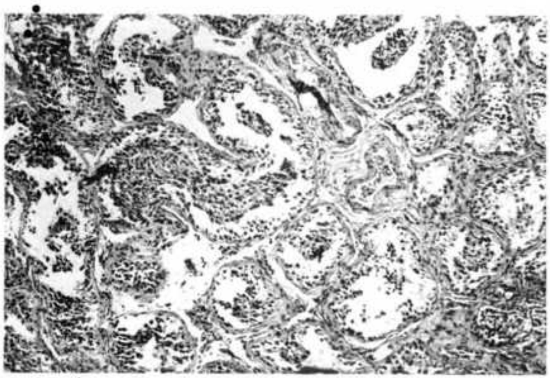


Fig. 1. Normal testicular biopsy from a 30-year-old man showing active spermatogenesis. HE. (× 80.)

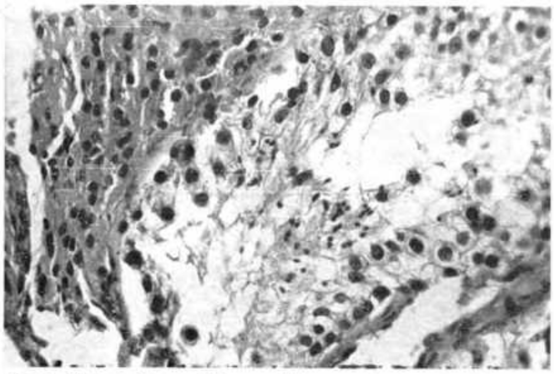


Fig. 2. Biopsy from a 55-year-old man prior to vasectomy, showing senile Leydig cell hyperplasia (upper left). HE. (× 360.)

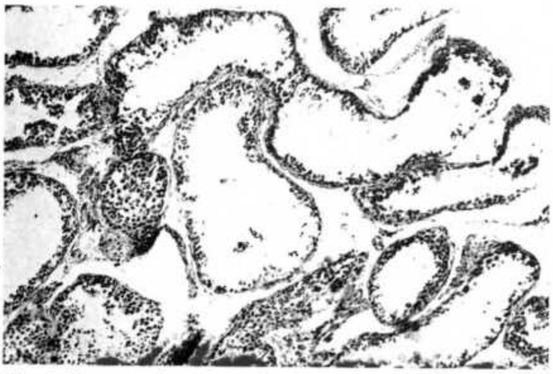


Fig. 3. Degeneration of germinal epithelium and arrested spermatogenesis in a young adult 1 month after vasectomy. Most of the tubules appear distended. HE. (×80.)

mean value has risen from 2·2 ± 0·4 ml/testis to 2·6 ± 0·5 ml/testis, an increase of about 18 per cent.

In the 10 subjects above the age of 50 years the total Leydig cell volume, which was already as high as 2·9 ± 0·7 ml/testis due to ageing, showed only a minor and inconsistent fluctuation after vasectomy. Although the number of cases is small, it appears that vasectomy does not significantly influence the Leydig cell content of the testis in older subjects, in contrast to the increase observed in the young.

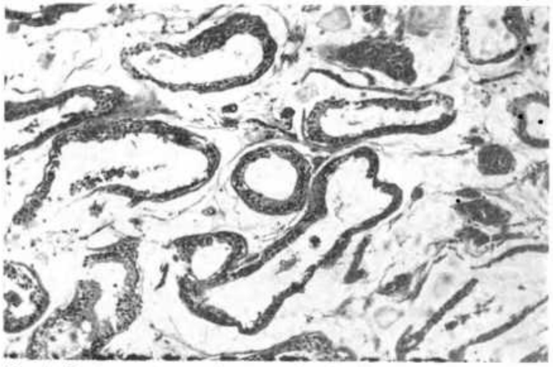


Fig. 4. Post-vasectomy degeneration in the seminiferous tubules of a male aged 54 years. HE. (× 80.)

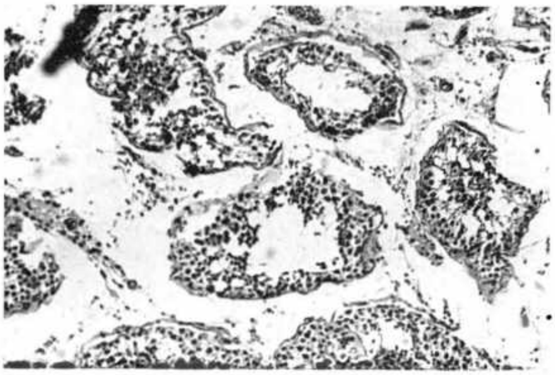


Fig. 5. Regenerated germinal epithelium and active spermatogenesis in a young adult 3 years after vasectomy. HE. (× 80.)

Table I: EFFECT OF VASECTOMY ON TESTICULAR VOLUME

Group	No. of cases	Testicular volume (ml) Before vasectomy	Testicular volume (ml) After vasectomy	P
Young (30–35 yr)	20	13·6 ± 5·1	13·4 ± 4·7	>0·10
Elderly (50–60 yr)	10	11·9 ± 6·5	10·0 ± 5·2	>0·05

Table II: EFFECT OF VASECTOMY ON TOTAL LEYDIG CELL VOLUME IN YOUNG ADULTS (30–35 YEARS)

Group	No. of cases	Absolute Leydig cell volume (ml/testis) Mean	Absolute Leydig cell volume (ml/testis) Range
Vasectomy cases	20		
Before vasectomy		2·2 ± 0·4	1·2–3·1
One month after vasectomy		2·5 ± 0·5	1·7–3·3
Recanalization cases 2–3½ years after vasectomy	10	2·6 ± 0·5	1·7–3·5

Discussion

In many parts of the world today vasectomy would rank amongst the most commonly performed elective surgical procedures. It may easily be presumed that it leads to no other consequence except sterility because there are hardly any postoperative complications or complaints. However, many apparently unrelated long term effects can often go unnoticed, and the question whether vasectomy merely interrupts the testicular outflow or produces, in addition, any subtle structural, endocrinal, immunological or other changes is well worth asking, particularly when vasectomy is being performed in such large numbers.

In the present study on human subjects widespread degeneration of the seminiferous tubules has been found in all the cases 1 month after vasectomy. Spermatogenesis naturally ceases. This conforms to our earlier observations in the dog where marked degenerative changes (Kothari et al., 1973) and histochemical alterations in the distribution of lipids, cholesterol, glycogen and enzymes have been found (Kothari and Mishra, 1973). The basal germ cells, however, escape this degeneration, either because they are furthest from the lumen or because they are the most primitive and undifferentiated. In any case, their preservation upholds the possibility of regeneration of the seminiferous tissue later on. Vasectomy also produces some thickening of the tunica propria of the seminiferous tubules. How this affects the functional qualities of the tunica—regulation of fluid exchange and maintaining adequate pressure for onward movement of tubular contents—is uncertain. A similar thickening of the tunica propria, however, occurs in several unrelated conditions of the testis associated with degeneration of the germinal tissue, e.g. Klinefelter's syndrome, exposure to X-rays or ionizing radiations etc. (Velardo, 1958).

That this post-vasectomy degeneration is followed by a spontaneous regeneration is now in no doubt. The testicular structure has been found to be essentially within normal limits, with active spermatogenesis, in subjects examined 2–3½ years after vasectomy. Recanalization is, therefore, not necessary to initiate the regenerative process, and the testis, after a lapse of time, seems to accommodate to its obstructed outflow. Whether the sperms formed in the vas-occluded testis (or the testis with congenital absence/obstruction of the vas) are functionally normal also seems doubtful, since Kubota (1969) has found, by electron microscopy, degenerative changes in the spermatids and sperms of vasectomized men. However, after the vas has been recanalized, successful pregnancies frequently do occur.

It would be reasonable to presume that this post-vasectomy degeneration results from an increase in the intraluminal pressure as the fluid accumulates behind the obstruction. Disparity amongst different species could possibly be related to the absorptive capacity of the epididymis which buffers any change in pressure. The absence of any inflammatory reaction, haemorrhage, etc., in all the cases clearly shows that the testicular changes are not due to any faulty operative technique or to an inadvertent interference with the blood supply.

Endocrine testis

It is obvious that in elderly persons or vasectomized individuals in whom spermatogenesis has lost its importance, the endocrine function of the testis still has a vital role to play and continues to do so even in advanced old age. We have therefore made a quantitative estimate of the total Leydig cell content before and after vasectomy in absolute terms (ml/testis), which makes the result independent of any change in testicular size. The accuracy of the method employed has already been experimentally demonstrated (Kothari et al., 1972).

In young healthy adults the total Leydig cell volume has been found to be 2·2 ± 0·4 ml/testis, with a range of 1·2–3·1 ml (*Table II*). Vasectomy has produced a modest but consistent increase in the total Leydig cell volume which has reached a mean value of 2·5 ± 0·5 ml/testis after 1 month. In subjects examined 2–3½ years after the operation the mean Leydig cell volume has increased significantly to 2·6 ± 0·5 ml/testis. Males above 50 years of age have shown a high Leydig cell content (2·9 ± 0·7 ml/testis) even without vasectomy. This seems to be a part of the ageing process and possibly reflects a pituitary-sponsored hyperplasia initiated by a negative feedback from a declining testosterone secretion (Kothari and Gupta, 1974). Vasectomy does not significantly alter this picture. It appears, therefore, that the elderly vasectomized male can have a larger than normal Leydig cell volume, but this seems to be the result of ageing rather than vasectomy—a fact which could have misled many earlier observers. It may well reflect a hypotestosteronism rather than hypertestosteronism, much like an iodine-deficiency enlargement of the thyroid. On the other hand, the consistent increase in Leydig cell volume in young adults is a direct result of vasectomy. A similar increase has been quantitatively demonstrated in dogs (Kothari and Mishra, 1972; Kothari et al., 1973). This is significant, although it must be admitted that an increase in the size of an endocrine gland does not necessarily imply an increase in hormone output.

The cause of post-vasectomy Leydig cell hyperplasia is uncertain. It may possibly involve some yet undefined humoral feedback from the degenerating seminiferous tubules to the anterior pituitary which could stimulate, through its gonadotropins, the endocrine Leydig cells or promote their differentiation from existing precursor cells (Johnsen, 1972). A continuous lysis of the sperms could keep the process going even when the germinal epithelium has recovered from its immediate post-vasectomy degeneration.

The final question still remains: Has vasectomy any real rejuvenating effect? The increase in Leydig cells observed by us, the rise in androgen-dependent constituents of the semen (fructose and acid phosphatase; Kothari, 1974) and the enhanced libido experienced by some vasectomized males do seem to uphold the possibility, but the fact that these changes are more evident in the young rather than the aged is discouraging. A long-term follow-up of vasectomized individuals and repeated testosterone estimations may help to resolve this interesting controversy.

References

AHMAD K. N., LENNOX B. and MACK W. S. (1969) Estimation of the volume of Leydig cells in man. *Lancet* 2, 461–464.

BAILLIE A. H. (1960) The biology of the Leydig cell: histochemical and histological changes following high epididymal obstruction. *J. Endocrinol.* **20**, 339–344.

HARRISON R. G. and MACMILLAN E. W. (1954) The effect of high epididymal obstruction upon the Leydig cell volume of rat testis. *J. Endocrinol.* **11**, 89–96.

HOUSSAY B. A. (1955) *Human Physiology*, 2nd ed. New York, McGraw-Hill, p. 682.

JOHNSEN S. G. (1972) Studies on pituitary testicular axis in male hypogonadism, particularly in infertile men with 'cryptogenetic' hypospermatogenesis. In: *Gonadotropins*. New York, Wiley–Interscience, pp. 593–608.

KOTHARI L. K. (1974) Unpublished observations.

KOTHARI L. K. and GUPTA A. S. (1974) Effect of ageing on the size, structure and total Leydig cell content of human testis. *Int. J. Fertil.* **20**. In the press.

KOTHARI L. K. and MISHRA P. (1972) Vasectomy and the endocrine function of the testis. *Lancet* **1**, 438.

KOTHARI L. K. and MISHRA P. (1973) Histochemical changes in the testis and epididymis after vasectomy. *Int. J. Fertil.* **18**, 119–125.

KOTHARI L. K., MISHRA P. and MISHRA R. K. (1973) Effect of bilateral vasectomy on the structure and function of testis. *Am. J. Surg.* **126**, 84–88.

KOTHARI L. K., SHRIVASTAVA D. K., MISHRA P. and PATNI M. K. (1972) Total Leydig cell volume and its estimation in dogs and models of testis. *Anat. Rec.* **174**, 259–264.

KUBOTA R. (1969) Electron microscopic study on the testis after vasectomy in rats and men. *Jap. J. Urol.* **60**, 373–397.

SMITH G. (1962) The effect of ligation of the vasa efferentia and vasectomy on testicular function in adult rat. *J. Endocrinol.* **23**, 385–399.

STEINACH E. (1927) Biological methods against the process of old age. *Med. J. Rec.* **125**, 77.

VELARDO J. T. (1958) *Essentials of Human Reproduction*. Oxford University Press, pp. 237–240.

Br. J. Surg. Vol. 62 (1975) 64–67

The relationship between ultrasound assessment and angiography in occlusive arterial disease of the lower limb

J. CHAMBERLAIN, E. HOUSLEY AND A. I. S. MACPHERSON*

SUMMARY

The Doppler ultrasound technique has been used to assess the haemodynamics of the peripheral circulation in patients with arterial disease. Using this method the resting pressure index and the response after exercise of the systolic pressure at the ankle was determined in 62 limbs.

Following exercise, four patterns of abnormal response to exercise were found and graded in severity from 1 to 4. A single aorto-iliac lesion was associated with a normal or slightly reduced resting pressure index but with a severe reduction of pressure (grade 3–4) after exercise. A single femoropopliteal lesion was usually associated with a low resting pressure index but only a slight (grade 1–2) fall after exercise.

A low resting pressure index and a severe post-exercise grade were found in patients with multiple occlusions. Disease of the profunda femoris artery was associated usually with both a low resting pressure index and a grade 3–4 post-exercise curve.

THE importance of functional measurements in the assessment of patients with peripheral vascular disease has been recognized in recent years. To be widely applicable, such a test must be not only accurate and reproducible but also easily and rapidly performed. Strandness et al. (1966), Yao et al. (1969) and Yao (1970) have reported favourably on methods based on the Doppler effect using a beam of ultrasound. With this technique it is possible to measure accurately the systolic blood pressure in small peripheral vessels, even when it is much reduced, and to observe the response of these pressures to exercise.

It seemed desirable to try to find out how far such a simple non-invasive technique could supplement or even replace the most established investigation in peripheral arterial disease, namely arteriography. The object of the present study was to use the ultrasound technique to make a functional assessment of patients with occlusive vascular disease affecting the lower limbs and to relate the findings to the appearances on angiography.

Patients

There were 31 patients in the study of whom 25 were male and 6 female. The ages ranged from 43 to 75 years. All the patients complained of intermittent claudication, often associated with absent ankle pulses and, in many cases, with other signs of ischaemia due to atherosclerotic occlusive vascular disease.

Methods

The systolic blood pressure was measured at the posterior tibial artery in the supine position using a Parks 810 Doppler Flowmeter and a pencil-shaped probe, from which is transmitted a beam of ultrasound of 10 MHz/second. The probe was used as a pulse detector and the systolic blood pressure measured with a sphygmomanometer cuff placed just above the ankle. The principles and use of this technique have been described by Strandness et al. (1966). The measurement was first made at rest and then every minute for 15 minutes after exercise. This was a simple two-step exercise, the patient stepping up to a stool and down at a fixed rate of 60 steps/minute for 5 minutes, or until he was forced to stop

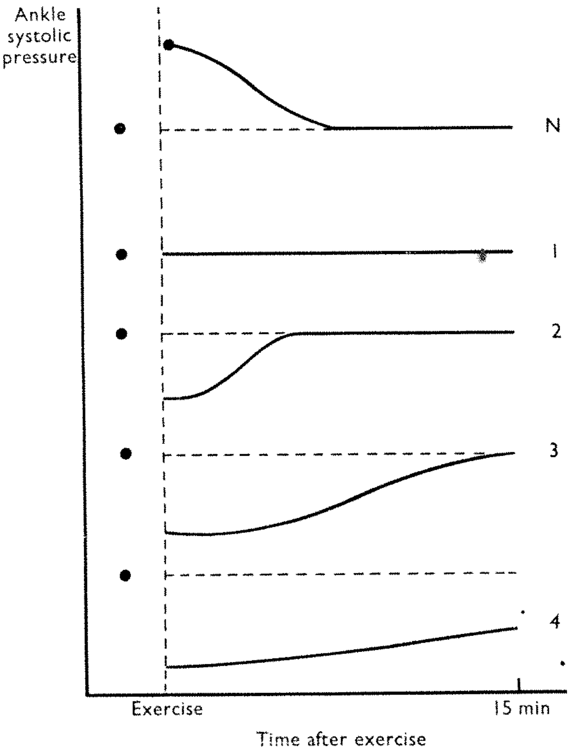


Fig. 1. Ankle systolic pressure after exercise. Normal and abnormal patterns of response.

---

* Peripheral Vascular Clinic, Royal Infirmary, Edinburgh. Present address of J. Chamberlain: Department of Surgery, Newcastle General Hospital, Newcastle upon Tyne.

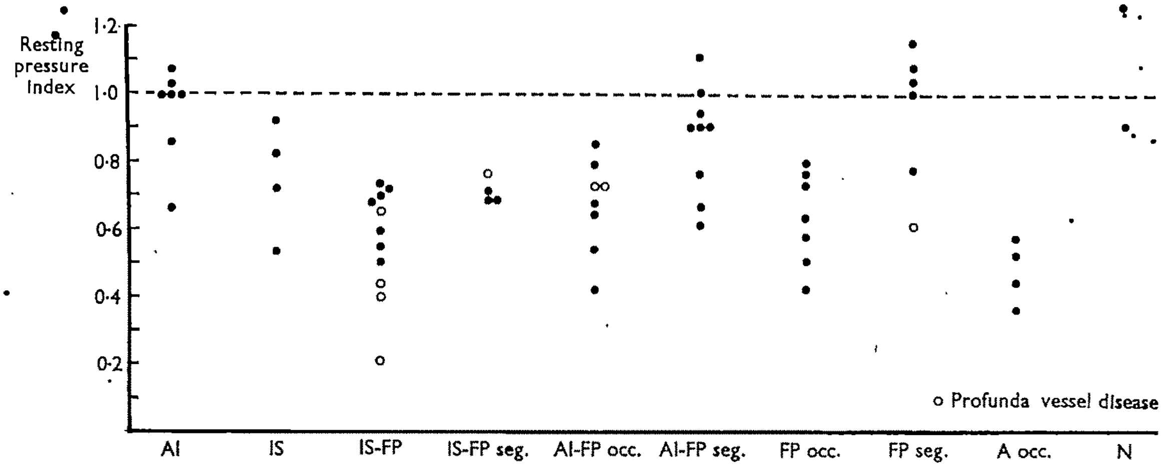


Fig. 2. Relation of resting pressure index to the anatomical patterns of arterial occlusions. *See Table II* for definition of abbreviations.

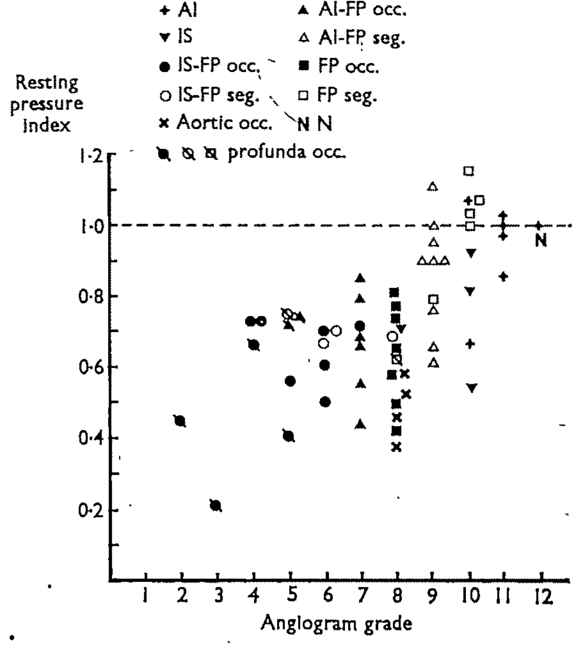


Fig. 3. Relation of resting pressure index to the angiographic score. *See Table II* for definition of abbreviations.

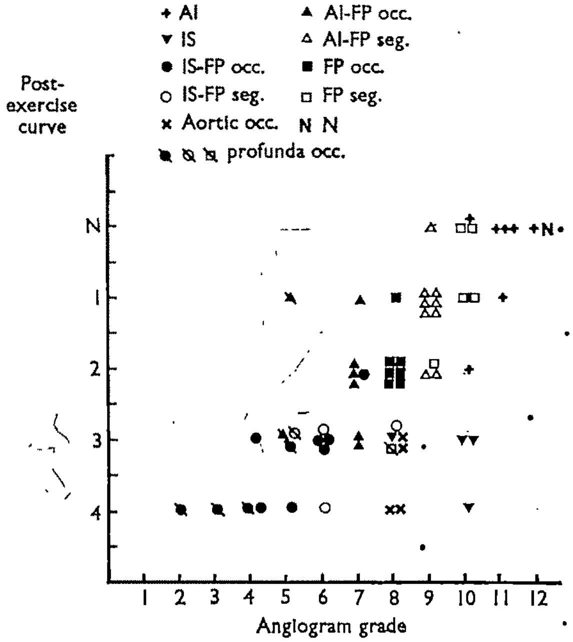


Fig. 4. Relation of the response of ankle systolic pressure to exercise to the angiographic score. *See Table II* for definition of abbreviations.

because of claudication. The ratio of the ankle systolic pressure to the brachial systolic pressure was calculated (pressure index). In normal subjects the value of the pressure index is almost always greater than 1·0 (Yao et al., 1969; Yao, 1970). In patients with occlusive vascular disease there is usually, though not always, a resting ankle systolic pressure index of less than 1·0.

After exercise in the normal subject there is an increase in leg blood flow and a fall in peripheral resistance because of dilatation of muscle vessels. The increased flow is greater than the fall in peripheral resistance, and the systolic pressure in the limbs tends to rise immediately after exercise. In occlusive vascular disease, although there is a rise in systemic blood pressure and cardiac output, the resistance of the lesion limits the increase in flow to the leg. The vasodilatation of muscle blood vessels diverts a large proportion of the limited flow and thus there is a fall in pressure in the distal arteries.

We have found four grades of severity of abnormal ankle pressure response after exercise (*Fig.* 1). In the type 1 curve there is no change in pressure after exercise although the resting pressure index may be normal or below normal. The type 2 curve shows a moderate fall in pressure after exercise with a fairly quick rise to the pre-exercise value. In the type 3 curve there is a moderate to severe fall in the resting value, and this

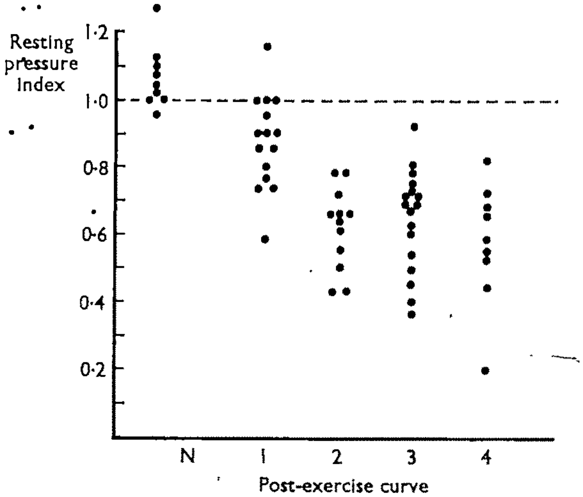


Fig. 5. Relation of the resting pressure index to the response of ankle systolic pressure after exercise.

Table I: NUMERICAL SCORING OF ANGIOGRAPHIC CLASSIFICATION

Artery	Condition	Score
Aorto-iliac	Normal	4
	Irregularity	3
	Stenosis	2
	Occlusion	0
Femoropopliteal	Normal	4
	Stenosis	2
	Occlusion	0
Profunda femoris	Normal	4
	Stenosis	2
	Occlusion	0

Table II: ATHEROSCLEROTIC LESIONS AS SEEN ON THE ANGIOGRAM IN 62 LIMBS

Lesion	No. of cases	Profunda vessel disease
Aorto-iliac (AI)	7	—
Iliac stenosis (IS)	4	—
Iliac stenosis and femoropopliteal occlusion (IS-FP occ.)	11	4
Iliac stenosis and femoropopliteal segmental disease(IS-FP seg.)	4	1
Aorto-iliac and femoropopliteal occlusion (AI-FP occ.)	8	2
Aorto-iliac and femoropopliteal segmental disease (AI-F Pseg.)	9	— —
Femoropopliteal occlusion (FP occ.)	7	
Femoropopliteal segmental disease (FP seg)	6	1
Aortic occlusion (A occ.)	4	—
Normal (N)	2	—

has returned to the pre-exercise value by the end of the 15-minute post-exercise monitoring period, and in type 4 there is a profound fall in ankle systolic pressure and the pressure has not returned to the pre-exercise value by the end of 15 minutes.

Angiograms were carried out by routine radiological methods by either the percutaneous femoral or translumbar route. The angiograms were then assessed by a method based on that described by Morton et al. (1967). Each segment was given a score varying from 0 to 4 (*Table I*), depending upon the type and extent of disease demonstrated. The assessment of this according to the pathology present is shown in *Table II*.

Results

Resting pressure index (*Fig*. 2)

A single aorto-iliac stenosis was usually associated with a normal or only slightly reduced index. The resting pressure index tended to be lower when there were extensive or multiple arterial occlusions, and particularly when the profunda femoris vessels were involved. In patients with iliac stenosis and femoropopliteal occlusions there was a significant difference ($P<0{\cdot}05$) in those with and without disease of the profunda femoris, but the considerable overlap makes the measurement of little value in the individual case. The resting pressure index and the angiographic scores are compared in *Fig*. 3 and a correlation is demonstrated which is highly significant ($P<0{\cdot}001$). Where radiographic involvement of the profunda vessels could be demonstrated there was also both a low resting pressure ratio and a low angiographic score.

Post-exercise pressure curves

The types of post-exercise curves are plotted against the angiographic score in *Fig*. 4. It is evident that a low angiographic score, indicating multiple occlusions, and disease of the profunda femoris vessels are both associated with a type 3 or type 4 post-exercise curve. The correlation between the type of curve obtained and the angiographic score is significant ($P<0{\cdot}001$). However, there is a group of 10 cases in which a type 3 or 4 curve is found with an angiographic score of 8–10. Eight of these cases were single aortic or aorto-iliac occlusions with normal femoropopliteal segments and all the aorto-iliac occlusions had a type 3 or 4 curve.

A clear correlation also exists between the resting pressure index and the type of post-exercise curve (*Fig*. 5).

Discussion

The technique described is atraumatic, easy to perform repeatable and requires no expensive recording apparatus. The general validity of the measurements appears to be confirmed by the significant correlation between the post-exercise pressure curves and the degree and extent of the occlusive process as measured by numerical scoring of the angiogram. The severity of the functional impairment in single aorto-iliac lesions is clearly demonstrated. The disparity between the functional measurement and angiographic score in such patients suggests that the scoring system underestimates the 'severity' of such lesions.

This study confirms the limit of the pressure index in patients with proximal lesions only. These patients may have a relatively high pressure index and the significance of the lesion only becomes evident on exercise.

In the few patients with proved narrowing of the profunda femoris artery (the main collateral vessel to the lower limb) the post-exercise pressures were always significantly lowered. However, the wide overlap between the various groups makes it impossible to use the technique as a method for defining the anatomical distribution of disease in an individual patient. This fact, together with the need for accurate knowledge of the anatomy of the lesions when planning surgery, means that the present technique cannot replace angiography but is a valuable supplementary investigation.

The technique provides an objective record of the functional importance of an occlusion in the main artery whether demonstrated clinically or radiologically. It is also of use in excluding or assessing the significance of peripheral vascular disease in doubtful or atypical cases of intermittent claudication without recourse to angiography, and finally it provides an easy and reliable test with which to assess progress of the disease or the effect of therapy.

References

MORTON D. L., EHRENFIELD W. K. and WYLIE E. J. (1967) Significance of outflow obstruction after femoropopliteal endarterectomy. *Arch. Surg.* **94**, 952–956.

STRANDNESS D. E. J., MCCUTCHEON E. P. and RUSHMER R. F. (1966) Application of a transcutaneous Doppler flowmeter in evaluation of occlusive arterial disease. *Surg. Gynecol. Obstet.* **122**, 1039–1045.

YAO S. T. (1970) Haemodynamic studies in peripheral arterial disease. *Br. J. Surg.* **57**, 761–766.

YAO S. T., HOBBS J. T. and IRVINE W. T. (1969) Ankle systolic pressures in arterial disease affecting the lower extremities. *Br. J. Surg.* **56**, 676–679.

Br. J. Surg. Vol. 62 (1975) 68–71

Phenol sympathectomy in the treatment of intermittent claudication: a controlled clinical trial

T. FYFE AND R. O. QUIN*

SUMMARY

Twenty-five patients with intermittent claudication were randomly allocated to treatment either by injection of phenol into the lumbar sympathetic chain or by injection of local anaesthetic subcutaneously. On the day after the injection, sympathectomy, assessed by skin temperature change, was achieved in 85 per cent of the phenol group.

At 1 month subjective improvement was claimed by 45 per cent of the patients in the sympathectomized group and by 64 per cent in the control group; at 3 months the figures were 25 and 45 per cent respectively.

Treadmill testing at two exercise loads showed no significant difference in claudication distance or stopping time between the two groups. Calf blood pressure response following exercise was not affected by sympathectomy.

There is no subjective or objective evidence that phenol sympathectomy improves intermittent claudication.

LUMBAR sympathectomy either by operation or by injection of phenol or alcohol is claimed to benefit patients with intermittent claudication (Smithwick, 1957; MacKenzie and Loewenthal, 1962; Reid et al., 1970), but this has been disputed (Richards, 1971). There is little objective evidence to support either claim, however, and there have been no controlled clinical trials reported.

Materials and methods

Twenty-five patients (24 males and 1 female) were included in the trial. All had a history of intermittent claudication which predominantly affected one leg and which had been stable for at least 3 months. They had palpable femoral pulses with diminished or absent pulses distally and all showed a drop in the calf blood pressure of the affected leg after exercise. The patients were randomly allocated to a 'phenol group' or to a 'control group'. Those in the phenol group were given an injection of 5 ml of 1 : 15 solution of phenol into the lumbar sympathetic chain at each of two levels by the method of Reid et al. (1970). The control group received lignocaine subcutaneously into the lumbar region on the affected side.

The assessment was made by a physician who did not know to which group the patients belonged. On two occasions, separated by at least a week, before injection and again at 1 month and 3 months after injection the patients were asked if there had been any change in the distance they could walk; they were exercised on a treadmill, and the blood pressure changes in the legs after exercise were measured.

Treadmill testing consisted of exercising at 2 m.p.h. at a 15° gradient followed by 2 minutes' rest, then exercising at 3 m.p.h. at 20°. The patient indicated the onset of claudication and stopped the treadmill when he felt compelled to do so. Three such tests were carried out at each visit with an interval of at least 30 minutes' rest between each test. Thus six estimates of time to the onset of claudication and stopping time were obtained for each patient before injection for comparison with six measurements after injection.

Systolic blood pressure changes in both legs were measured following exercise at 3 m.p.h. at 20° once at each visit. The blood pressure was measured using sphygmomanometer cuffs placed around the calves just below the tibial tuberosities and an ultrasonic Doppler instrument to detect the onset of flow in the posterior tibial or dorsalis pedis arteries. Measurements were made every 2 minutes for a period of 10 minutes and again at 15 minutes after exercise. The blood pressure in the affected leg was expressed as a ratio of that in the other leg. The blood pressure in the right arm was also measured at rest and the leg : arm blood pressure ratio calculated. All blood pressures were recorded with the patient semi-recumbent in a reclining chair. The leg pressure in the leg : arm blood pressure ratio is thus subject to an increased hydrostatic effect, which will increase the ratio in these patients relative to the ratio as derived in other reports, where the patient is horizontal.

The effectiveness of the sympathectomy in the phenol group was assessed by the surgeon who allocated the patients to the treatment group and who carried out the injections. This was done by comparing the mean temperature at ten sites on the dorsum of each foot after exposure of the limbs to room temperature for half an hour. The temperatures were measured with a thermocouple before injection, on the day after and at 3 months after injection.

Student's *t*-test was used to analyse the significance of results.

Results

Thirteen patients were randomly allocated to the phenol group and 12 to the control group. Eleven patients in the phenol group had a successful

---

* Departments of Medicine and Surgery, Western Infirmary, Glasgow.

Address for reprints: T. Fyfe, Department of Medicine, Vale of Leven District General Hospital, Alexandria, Dunbartonshire G83 0UA

Table I: TEMPERATURE DIFFERENCES BETWEEN LEGS AND CLINICAL PRESENCE OR ABSENCE OF SYMPATHECTOMY AFTER INJECTION OF PHENOL

Case no.	Temperature difference before injection (°C)	Day after injection: Temperature difference (°C)	Day after injection: Clinical sympathectomy	3 Months after injection: Temperature difference (°C)	3 Months after injection: Clinical sympathectomy
1	−0·5	+6·8	+	+1·6	+
2	−0·3	+2·0	+	0	−
3	+0·8	+3·8	+	+3·2	+
4	−0·5	+6·3	+	+2·0	+
5	0	+5·7	+	+0·5	−
6	−0·7	+3·6	+	+0·4	−
7	+0·2	+4·9	+	+2·3	+
8	−0·2	+6·7	+	+0·6	−
9	+0·5	+3·0	+	+0·6	−
10	−1·1	+4·0	+	+0·4	−
11	−0·5	+5·5	+	+1·3	−
12	−0·3	−0·2	−		−
13	−0·2	−0·5	−		−

Table II: COMPARISON OF GROUPS (MEAN±s.d.)

Group	No. of patients	Age (yr)	Claudication time (sec): 2 m.p.h. at 15°	Claudication time (sec): 3 m.p.h. at 20°	Stopping time (sec): 2 m.p.h. at 15°	Stopping time (sec): 3 m.p.h. at 20°	Leg : arm blood pressure ratio
Phenol	11	63±5	73±31	37±14	122±56	52±17	0·74±0·21
Control	11	58±8	80±35	38±9	129±60	56±10	0·82±0·24

Table III: CLAUDICATION TIMES BEFORE AND AFTER INJECTION TOGETHER WITH THE PROPORTION OF PATIENTS SHOWING SIGNIFICANT IMPROVEMENT OR DETERIORATION

	2 m.p.h. at 15°				3 m.p.h. at 20°			
	Claudication time (sec, mean±s.d.)		Proportion of patients (%)		Claudication time (sec, mean±s.d.)		Proportion of patients (%)	
Group	Before	After	Improved	Worse	Before	After	Improved	Worse
Phenol	73±31	91±40	50	0	37±14	40±18	33	11
Control	80±35	161±144	55	0	38±9	47±12	40	0

Table IV: STOPPING TIMES BEFORE AND AFTER INJECTION TOGETHER WITH THE PROPORTION OF PATIENTS SHOWING SIGNIFICANT IMPROVEMENT OR DETERIORATION

	2 m.p.h. at 15°				3 m.p.h. at 20°			
	Stopping time (sec, mean±s.d.)		Proportion of patients (%)		Stopping time (sec, mean±s.d.)		Proportion of patients (%)	
Group	Before	After	Improved	Worse	Before	After	Improved	Worse
Phenol	122±56	126±64	18	18	52±17	48±20	20	20
Control	129±60	195±137	60	10	56±10	58±14	9	18

sympathectomy judged clinically and by a temperature difference of at least +2 °C between the limbs (*Table I*) on the day after injection. The other 2 patients in the phenol group did not show any change in temperature in the treated limb and the results in these patients will be considered separately. For analysis the phenol group was composed of the 11 patients who had a successful sympathectomy on the day after injection. It can be seen (*Table I*) that the cutaneous vasodilatation declined and at 3 months only 4 of these patients had a sympathectomy detectable clinically. However, the treated limb was relatively warmer in all cases at 3 months ($P < 0{\cdot}05$ in 8 out of 11 cases). In the control group 1 patient defaulted after receiving the placebo injection, leaving 11 patients in the control group for analysis. There was no significant temperature change following placebo injection.

Table II compares the phenol group with the control group. The groups are well matched in terms of disease severity judged by treadmill testing and by the leg : arm blood pressure ratio. The mean age of the patients in the control group is slightly less than that of the phenol group but this difference is not significant.

In the phenol group 45 per cent (5 patients) claimed to be improved 1 month after injection and at 3 months 25 per cent (2 out of 8; 3 patients refused to return for further treadmill testing). This compares with 64 and 45 per cent at 1 month and 3 months in the control group. If the patient who defaulted from the control group is regarded as a failure the percentage claiming improvement would fall to 58 per cent at 1 month and 42 per cent at 3 months.

Both the patients who had an unsuccessful sympathectomy following phenol injection said they were

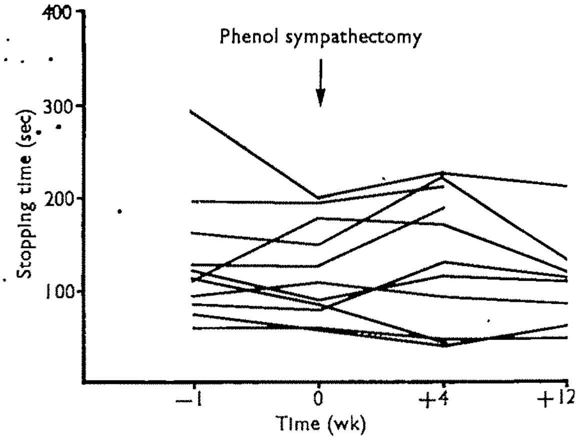


Fig. 1. Mean stopping times for individual patients in the phenol group at each series of assessments after exercise at 2 m.p.h. and 15°.

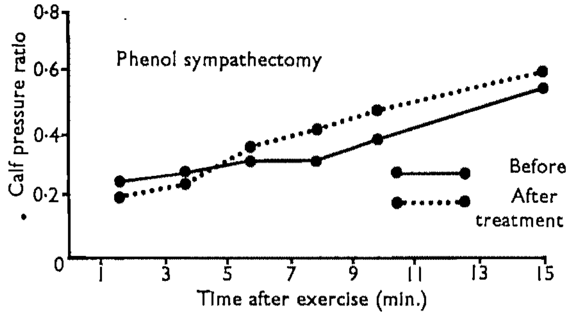


Fig. 2. Mean calf blood pressure ratio for the phenol group following exercise at 3 m.p.h. and 20°.

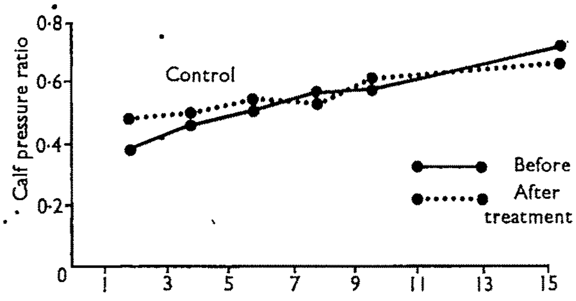


Fig. 3. Mean calf blood pressure ratio for the control group following exercise at 3 m.p.h. and 20°.

improved, but even if these patients were included the percentage claiming improvement would still not be better than that in the control group, being 54 per cent at 1 month and 40 per cent at 3 months. Of the 4 patients with a clinical sympathectomy still apparent at 3 months, 2 claimed improvement in walking distance.

The results for treadmill assessment are shown in *Tables III* and *IV*. Only the mean results before and after treatment are shown because it was found that analysing the results for each series of assessments did not alter the overall picture. This is illustrated in *Fig*. 1 which shows the mean stopping time for each patient in the phenol group at 2 m.p.h. and a 15° gradient at each visit. The phenol group were not significantly better than the control group in any treadmill assessment. None of the 4 patients who still had a clinical sympathectomy at 3 months showed improvement on treadmill testing.

The calf blood pressure response to exercising at 3 m.p.h. at 20° is shown for the phenol group in *Fig*. 2 and for the control group in *Fig*. 3. Standard deviations were large and are not shown. Injection did not alter the response in either group and there was no significant difference between the groups.

Discussion

A clinically obvious sympathectomy with a temperature increase of at least 2 °C relative to the other limb was achieved on the day following injection in 85 per cent of the patients injected with phenol. At 3 months after injection, only 4 patients had a clinically obvious sympathectomy, but there was evidence of some residual effect in the remainder since all showed an increase in temperature relative to the other limb. It is known that the blood flow response following surgical sympathectomy is greatest initially and declines thereafter (Lynn and Barcroft, 1950). The results in the patients with a sustained clinically obvious sympathectomy, were, however, no different from the others.

We have shown that sympathectomy does not improve intermittent claudication in this selected group of patients with femoropopliteal disease. Indeed it should be noted that the subjective results in our control group are as good as those claimed by others for sympathectomy in patients with a similar level of peripheral arterial disease (Mavor, 1955; MacKenzie and Loewenthal, 1962; King et al., 1964; Myers and Irvine, 1966; Reid et al., 1970). It is well known that such patients exhibit a marked placebo response (Hamilton and Wilson, 1952) and account should be taken of this when assessing results of sympathectomy.

We conclude that phenol sympathectomy produces no objective benefit in intermittent claudication.

References

HAMILTON M. and WILSON G. M. (1952) The treatment of intermittent claudication. *Q. J. Med.* **21**, 169–183..

KING R. D., KAISER G. C., LEMPKE R. E. and SHUMACKER H. B. (1964) Evaluation of lumbar sympathetic denervation. *Arch. Surg.* **88**, 36–47.

LYNN R. B. and BARCROFT H. (1950) Circulatory changes in the feet after lumbar sympathectomy. *Lancet* **1**, 1105–1108.

MACKENZIE D. C. and LOEWENTHAL J. (1962) Lumbar sympathectomy and claudication distance. *Surg. Gynecol. Obstet.* **115**, 303–311.

MAVOR G. E. (1955) Intermittent claudication and sympathectomy. *Lancet* **2**, 794–796.

MYERS K. A. and IRVINE W. T. (1966) An objective study of lumbar sympathectomy. I. Intermittent claudication. *Br. Med. J.* **1**, 879–883.

REID W., KENNEDY WATT J. and GRAY T. G. (1970) Phenol injection of the sympathtiic chain. *Br. J. Surg.* **57**, 45–50.

RICHARDS R. L. (1971) Lumbar sympathectomy for chronic occlusive aterial disease. *Am. Heart J.* **81**, 735–737.

SMITHWICK R. H. (1957) Lumbar sympathectomy in the treatment of obliterative vascular disease of the lower extremities. *Surgery* **42**, 415–430.

Br. J. Surg. Vol. 62 (1975) 72–76

A clinical trial designed to discover if the primary treatment of varicose veins should be by Fegan's method or by an operation

F. S. A. DORAN AND MARY WHITE*

SUMMARY

1. *The current practice of operating upon patients with varicose veins as the treatment of choice costs more than £15 millions a year.*

2. *The bulk of this expense is due to the length of time that patients are kept in the ward. If they were treated as outpatients, either by Fegan's method or by operation, the cost would be reduced to one-tenth of what is now spent. Even if the operation were done on a 'short-stay' basis the cost would be reduced to one-third or less.*

3. *Although the long term results of Fegan's method are uncertain there is no doubt that it gives better immediate results than an operation. Moreover, there is no particular type of varicosity or shape of limb which precludes its use.*

FROM 1855 to 1905 varicose veins were treated by sclerosing injections. Ligation at the saphenofemoral junction and stripping dates from 1905. It did not become the standard treatment in this country until about 1950. Now it is the most frequently performed operation in general surgery. Each year in England and Wales 150 000 patients are operated on for varicose veins (Lees, 1969) at a cost of more than £15 millions.

The problem is to decide whether these patients can be treated more cheaply by using Fegan's compression-injection method of sclerotherapy and diverting the money saved to some other surgical task.

If Fegan's method is to become the primary treatment of choice it must be proved that it is as good a treatment as the operation of saphenofemoral ligation and stripping of the long saphenous trunk.

It has been asserted that a patient with varicose veins can be treated by Fegan's method at the cost of £9·77 per head as compared with £44·22 per head if he were operated upon (Piachaud and Weddell, 1972). At its face value this represents an annual saving in England and Wales of over £5 millions.

Under prevailing surgical management it would save nearly three times that amount because the calculation made by Piachaud and Weddell (1972) rested on the fact that the patients who were operated on were sent home in 3·7 days. By contrast, as the authors point out, the latest 'mean national length of stay for varicose vein cases' ranges from 7·5 to 15·7 days, with an average of 11·7 days. This average length of stay in the ward coincides closely with the official figure of 10·5 days (Lees, 1969). At the present time in the Birmingham region 10 days as an inpatient costs £110 (Wall, 1973), and an actuarial analysis by the same regional board found that the average cost per operation was £13·30, inclusive of the pay of the doctors, the nurses, the domestics and 'others', and covering the cost of drugs, dressings and equipment. As a round figure, therefore, the cost of operating on a patient with varicose veins, taking England and Wales as a whole, is about £125.

Piachaud and Weddell (1972) calculated that the cost of the operation alone was £12, which coincides closely with the figure given above of £13·30. This leaves little doubt that the financial disadvantage of the operative method is almost entirely due to the time spent in the ward. The great financial advantage of Fegan's method, which is an outpatient treatment, rests upon this fact.

However, operation can also be performed on outpatients, as has been found both in North America (McPheeters, 1945) and in Britain (Stevens and Dudley, 1961). This practice would virtually abolish the financial disadvantage of treating varicose veins by operating on them.

Before this issue can be decided, properly constructed clinical trials must be carried out or the patients may suffer. Finance must not be the overriding factor. According to Piachaud and Weddell (1972) and to Seddon (1973) the two methods being compared in this trial are of equal merit.

Design of the trial

The present trial was arranged as a random series. Fegan's method was used on all the patients born in a year with an even number, while those born in a year with an odd number were operated upon.

Patients who were operated on were not managed as outpatients because to do so would tend to limit the operation to stripping of one saphenous vein. Clinically, this would have biased the trial in favour of Fegan's method because some patients need more than one long saphenous vein stripped. Therefore the patients were kept in hospital for 2 days because there is no limit to the amount of surgery possible on this basis (Doran et al., 1972).

To avoid confusion the comparison between the two methods was based on whether additional treatment was prescribed at the end of the first year and again at the end of the second year after treatment. Either additional treatment was given or it was not. Two years was chosen as the length of the trial. It is well known that with benign conditions of low morbidity it is difficult to maintain an efficient follow-up for longer.

---

* Mid-Worcestershire Hospitals of Bromsgrove and Kidderminster.

Method of injection-compression

The method used in this trial followed that of Fegan closely, except that ethamolin was used throughout. The quantity injected at each site was 0·5–1 ml. Not more than three or four sites were injected at the same visit into one limb (Fegan, 1964). The 'empty vein' technique recommended by Fegan (1960) was used routinely. There were no overdose effects.

The compression was obtained by bandaging a Sorbo rubber pad over the site of the injection and the application of a full length two-way-stretch elastic stocking over the bandages, held up where needed by a suspender belt, and worn day and night (Fegan, 1965).

Furthermore, the patients were instructed to walk 3 miles a day and to avoid standing (Fegan, 1965). The bandaging was examined at the hospital each week. At these visits the previous injection sites were examined and any additional injections required were given. Compression over the injection sites was maintained for 6 weeks at least after the last injection.

Before taking the final decision that the treatment was complete the patients were told to remove the stockings and bandages 2 days before they were due to be seen and to take a bath, replacing the stockings only. In this way the skin, corrugated by the bandages, has time to become smooth, which makes the final assessment much easier. If no additional injections were needed the elastic stockings alone were reapplied for a further 6 weeks, when the stockings were discarded and the patient followed up at increasing intervals up to 2 years from the start of the treatment.

Patients

Because the division and ligation of the incompetent perforating veins in the leg which cause ulceration are so uniformly successful in healing the ulcer it was considered unjustifiable to include such cases in the trial. Therefore, all patients presenting with an open varicose ulcer were excluded. This series numbers 331 patients with varicose veins uncomplicated by ulceration. Of this total, 182 patients were treated primarily by Fegan's method and 149 were operated upon. In the Fegan group 98 patients had bilateral varicose veins and in 84 the varicosities were confined to one leg. In the group who underwent operation 73 had bilateral varicose veins and in 76 they were unilateral. Presented as individual limbs, the Fegan group contains 280, and the operative group 222, making a total of 502 limbs for the whole series.

Table I: RESULTS AT THE END OF THE FIRST YEAR

			Limbs examined		Additional treatment	
Treatment	Total limbs	No. lost	No.	%	No.	%
Fegan	280	49	231	82·5	56	24·2
Operation	222	26	196	88·3	88	44·8

Table II: EFFECT OF FOLLOW-UP LOSSES ON RESULTS: χ^2 TEST

	Observed no. of failures, maximum possible		Observed no. of failures, minimum possible	
Result	Fegan	Operation	Fegan	Operation
Observed successes	224	134	175	108
Expected successes	199·68	158·32	157·85	125·15
Observed − expected	+24·32	−24·32	+17·15	−17·15
(Difference)^2 + expected	2·9670	3·7428	1·8633	2·3501
Observed failures	56	88	105	114
Expected failures	80·32	63·88	122·15	96·85
Observed − expected	−24·32	+24·32	−17·15	+17·15
(Difference)^2 + expected	7·7376	9·3037	2·4070	3·0367
χ^2	23·7511		9·6571	
P	0·01		0·01	

Table III: EFFECT OF FOLLOW-UP LOSSES ON RESULTS: χ^2 TEST

	Observed no. of failures, maximum for Fegan, minimum for operation		Observed no. of failures, minimum for Fegan, maximum for operation	
Result	Fegan	Operation	Fegan	Operation
Observed successes	224	108	175	134
Expected successes	185·18	146·82	172·35	136·65
Observed − expected	+38·82	−38·82	+ 2·65	−2·65
(Difference)^2 + expected	8·1379	10·2642	0·0410	0·0517
Observed failures	56	114	105	88
Expected failures	94·82	75·18	107·65	85·35
Observed − expected	−38·82	+38·82	−2·65	+2·65
(Difference)^2 + expected	15·8932	20·0451	0·0652	0·0823
χ^2	54·3404		0·2402	
P	0·01		0·10	

Results

As far as possible the observations made in this trial will be reported as the number of limbs treated. In patients with bilateral varicose veins the severity and the site of the varicosities in the two limbs seldom match. Furthermore, after a patient with bilateral varicosities has been treated one limb may be a success and the other a failure.

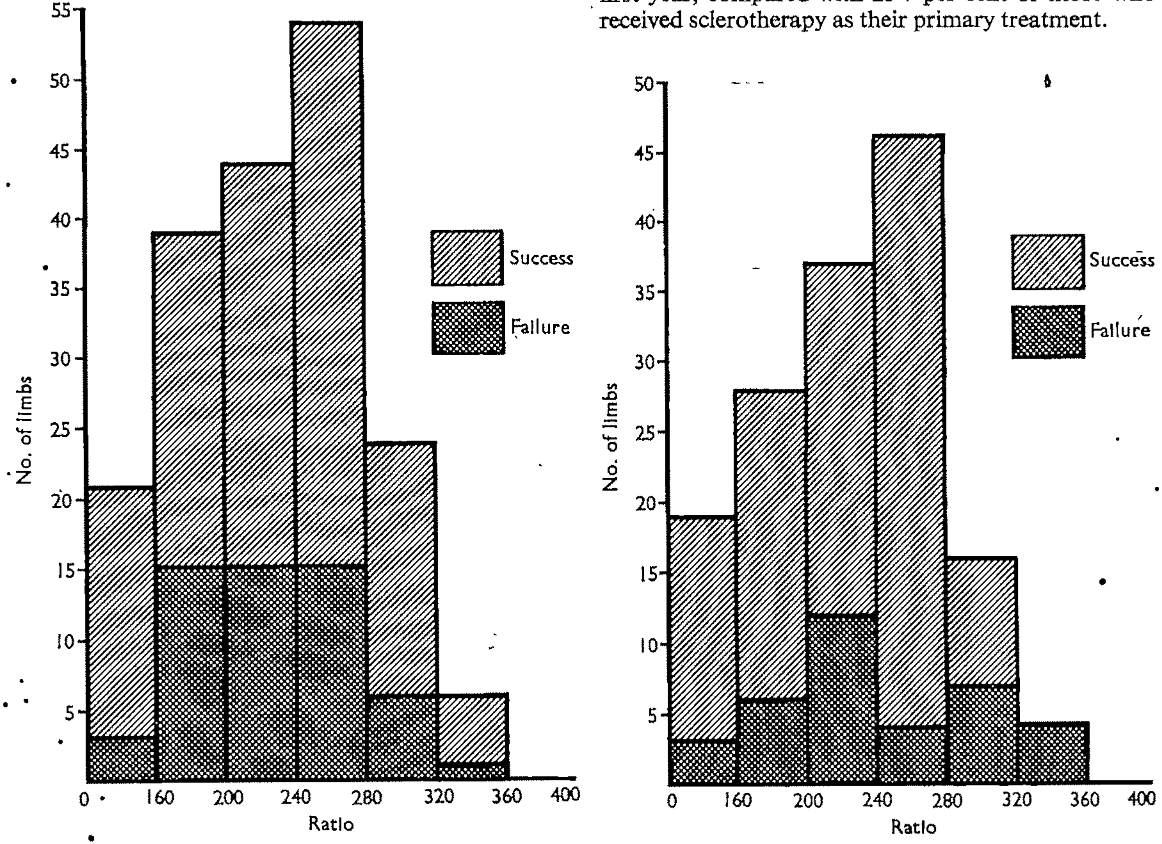
The results at the end of the first year are set out in *Table I.* The interpretation of this table is made difficult by the 75 limbs which, for a variety of reasons, were 'lost'. There are four possibilities:

1. All the 75 limbs which were 'lost' could have been successes.
2. All the 75 limbs which were 'lost' could have been failures.
3. The 49 limbs in the Fegan group which were 'lost' could have been successes but the 26 limbs in the operative group might have been failures.
4. The 26 limbs in the operative group which were 'lost' could have been successes and the 49 limbs in the Fegan group which were 'lost' could have been failures. *Tables II* and *III* show the calculation of χ^2 for each of these four possibilities.

It will be seen that except for the last contingency where all the 26 limbs in the operative group which were 'lost' are successes, and all the 49 limbs in the Fegan group which were 'lost' are failures, the Fegan method is superior to the operative method with values for P of less than 0·01. In the fourth permutation the two methods are equal in value. It is likely, therefore, that the initial response of varicose veins to compression-sclerotherapy is better than that to operation.

Table IV sets out the results at the end of the second year. They are of interest but of little value. They are of interest because they suggest that performing an operation before administering a course of sclerotherapy does not improve the results of sclerotherapy on its own. However, they are of little value because the efficiency of the follow-up during the second year fell from 85·1 to 66·9 per cent, the number of limbs 'lost' increasing from 75 to 166.

Table V shows an attempt to discover if pati'two whose varicose veins were mainly due to incompetents at the sephenofemoral junction, judged by the ence tourniquet' and calf exercise tests, ought to be treated primarily by operation. This is not the case; 49·6 per cent of the limbs on which a long saphenous stripping was done required Fegan injections at the end of the first year, compared with 23·7 per cent of those who received sclerotherapy as their primary treatment.



a *b*

Fig. 1. Results of sclerotherapy in relation to the configuration of the limbs. The limbs with the most slender thighs are represented by the column on the far left: those with the most bulky thighs by the column on the far right. *a*, At the end of the first year the failures were not concentrated amongst those with fat thighs and short legs. *b*, Results at the end of the second year supports the view that good results can be obtained on fat short legs if enough care is taken with the technique.

Table IV: RESULTS AT THE END OF THE SECOND YEAR

Treatment	Total limbs	No. lost	Limbs examined		Additional treatment	
			No.	%	No.	%
Fegan	280	102	178	63·6	39	21·3
Operation	222	64	158	71·2	26	16·4

There is no statistical difference between the two methods. Nearly half of the patients in the operation group had received a course of injections at the end of the first year.

Table V: SITES OF MAIN VALVULAR INCOMPETENCE

Vessels needing treatment	Fegan	Operation
Long saphenous vein alone	184 (23·7%)	149 (49·6%)
Long and short saphenous veins	20 (45·0%)	12 (33·3%)
Long saphenous and leg perforating veins	9 (11·1%)	25 (28·0%)
Long and short saphenous veins with leg perforating veins	None	9 (33·3%)
Short saphenous vein alone	10 (30·0%)	None
Leg perforating veins alone	1 (0·0%)	1 (0·0%)
Hunter's canal perforating vein alone	7 (14·3%)	None

Percentages in parentheses are the proportion in each group needing additional treatment at the end of the first year.

Table VI: EFFECT OF SITE OF THE VARICOSITIES

Site of varicosities	Fegan	Operation
Both thigh and leg	121 (30·6%)	122 (51·6%)
Knee and leg	107 (20·5%)	71 (40·8%)
Thigh only	3	3

Percentages in parentheses are the proportion in each group needing additional treatment at the end of the first year.

Table VII: EFFECT OF PRELIMINARY OPERATION ON NUMBER OF INJECTIONS NEEDED

No. of injection visits	Primary Fegan injections, clinical trial limbs (%)	Postoperative Fegan injections	
		Clinical trial limbs (%)	141 'Extra' limbs (%)
1– 5	64·6	82·4	77·7
6–10	23·8	14·0	19·0
11+	11·6	3·6	3·3

Table VI records the results of operation and Fegan's method in relation to the site of the varicosities. Fewer limbs treated primarily by sclerotherapy required additional treatment at the end of the first year than those operated upon, irrespective of site.

Fig. 1 analyses Fegan's (1963) opinion that obesity makes it hard to get a good result with sclerotherapy because maintaining the required compression is extremely difficult. This problem was tested by subtracting the circumference of the calf from that of the thigh and dividing the difference by the length of the limb. This measures the configuration of the limb. The figures show that although technically difficult, good results can be obtained on short limbs with very fat thighs.

Finally, the possibility that fewer injections would be needed per limb if a preliminary operation had been carried out was examined. This was suggested more than 20 years ago (McElwee and Maisel, 1947), but Fegan (1963) denies it.

In 1968 Reid and Rothnie reported from Reading a series of 974 patients (1358 limbs) treated by sclerotherapy with encouraging results. Now, for about 10 per cent, where the whole limb is involved from the groin to the ankle at a high pressure, limited surgery is carried out on a 'short-stay' basis prior to sclerotherapy (Rothnie, 1973).

Table VII details the number of visits for injections paid by the patients who were treated primarily by Fegan's method and by those who, having been operated upon, needed injections for residual or recurrent varicosities. The results support the opinion that a preliminary operation reduces the number of injections required subsequently. The results in a further 141 limbs, which were all operated on before the start of this trial and all needing Fegan injections for residual and recurrent varicosities, also support this view.

Conclusions

1. The initial response of varicose veins is better if Fegan's method is used than if they are operated upon.
2. Fegan's method is not contra-indicated by primary saphenofemoral incompetence or by fat thighs provided that, in the latter case, great care is taken with the technique.
3. Which method is better in the long run may never be known owing to the great difficulty of maintaining the efficiency of the follow-up for more than a short time.
4. It is likely that preliminary operation reduces the number of injections required subsequently.
5. The policy of treating varicose veins initially by Fegan's method will probably save money, beds and theatre time, without any detriment to the patient.

References

DORAN F. S. A., WHITE M. and DRURY M. (1972) The scope and safety of short-stay surgery in the treatment of groin herniae and varicose veins. *Br. J. Surg.* **59**, 333–339.

FEGAN W. G. (1960) Continuous uninterrupted compression technique of injecting varicose veins. *Proc. R. Soc. Med.* **53**, 837–840.

FEGAN W. G. (1963) Continuous compression technique of injecting varicose veins. *Lancet* **2**, 109–112.

FEGAN W. G. (1964) The treatment of varicose veins during pregnancy. *Pacif. Med. Surg.* **72**, 274–279.

FEGAN W. G. (1965) Injection with compression as a treatment for varicose veins. *Proc. R. Soc. Med.* **58**, 874–876.

LEES W. (1969) Symposium on short-stay surgery. Birmingham Regional Hospital Board. Department of Health and Social Security contribution.

MCELWEE R. S. and MAISEL B. (1947) Study of results of surgical treatment of varicose veins. *Ann. Surg.* **126**, 350–357.

MCPHEETERS H. O. (1945) Sapheno-femoral ligation with immediate retrograde injection. *Surg. Gynecol. Obstet.* **81**, 355–364.

PIACHAUD D. and WEDDELL J. M. (1972) The economics of treating varicose veins. *Int. J. Epidemiol.* **1**, 287–294.

REID R. G. and ROTHNIE N. (1968) Treatment of varicose veins by compression sclerotherapy. *Br. J. Surg.* **55**, 889–895.

ROTHNIE N. (1973) personal communication.

SEDDON J. (1973) The management of varicose veins. *Br. J. Surg.* **60**, 345–347.

STEPHENS F. O. and DUDLEY H. A. F. (1961) The organisation for out-patient surgery. *Lancet* **1**, 1042–1044.

WALL M. (1973) Personal communication. Statistical Department, Birmingham Regional Hospital Board.

Br. J. Surg. Vol. 62 (1975) 77–79

Secondary involvement of the penis by rectal cancer

B. I. REES*

SUMMARY

Two cases of metastasis to the penis from a primary rectal carcinoma are described. The clinical features, treatment and prognosis together with the probable modes of metastasis are discussed. All previously reported cases of penile metastasis from the rectum are reviewed.

It is suggested that contrary to previous reports the prognosis is not uniformly poor and hence a more aggressive attitude to treatment should be adopted. Metastatic lesions in the penis should also be considered as a cause of urinary obstruction following abdominoperineal excision of the rectum.

SECONDARY carcinoma of the penis is rare. Abeshouse and Abeshouse (1961) collected 138 cases from the literature and added 2 cases of their own. The primary sites of origin are in order of frequency: genitourinary 75 per cent, gastro-intestinal 18 per cent and other sites 7 per cent. The first case of metastasis to the penis from a primary rectal neoplasm was reported by Eberth in 1870. Since then only a further 18 authenticated cases have been recorded in the literature and only one report can be found in the British literature. Two further cases are reported here, both of which followed abdominoperineal excision of the rectum and both presented with perineal pain and urinary obstruction.

Case reports

Case 1: A 41-year-old male had an abdominoperineal excision of the rectum for a low rectal carcinoma in May 1971. There was no evidence of metastasis at operation. Postoperatively he made a good recovery although the perineal wound was slow to heal. Histological examination of the specimen (*Fig.* 1) showed a well-differentiated adenocarcinoma which had invaded the tissues outside the bowel wall, and tumour was found in the lymph nodes along the vascular bundles.

The patient remained well until March 1972, when he had recurrent episodes of ureteric colic and also pain in the perineal scar. The ureteric colic settled after the passage of a stone and an intravenous pyelogram at this time was normal. However, pain in the perineal scar was continuous and severe so that the scar was excised in September 1972. Histology of this specimen was not obtained.

He remained moderately well until April 1973, when he developed hesitancy of micturition, a poor stream and passage of small amounts of urine. This culminated in an episode of acute retention which was treated by catheterization. When the catheter was removed urine was passed spontaneously. A repeat intravenous pyelogram was normal.

In July 1973 cystoscopy revealed urethral stenosis in the urethral bulb. During dilatation of the stricture a large indurated area was felt in the corpora cavernosa. The dilatation resulted in some transient improvement, but 2 months later he again developed acute retention of urine. At this time, when the prepuce was retracted, there were four painless nodular swelling on the glans penis. The body of the penis was hard but there was no true priapism and the inguinal glands were not palpable. Catheterization and urethral dilatation were performed. Excision biopsy of the nodules showed adenocarcinoma compatible with metastasis from the rectum (*Fig.* 2).

The patient was commenced on 5-fluorouracil. After a week of this, an attempt at removal of the catheter was unsuccessful. At present he is alive with an indwelling catheter 33 months after his original abdominoperineal excision and 8 months after penile metastases were diagnosed.

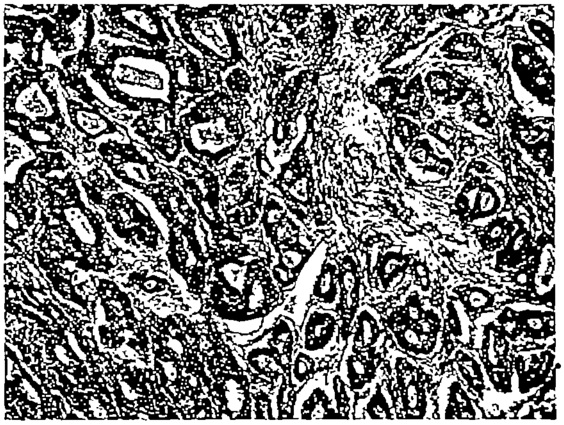


Fig. 1. *Case* 1. Histological section showing primary adenocarcinoma of the rectum.

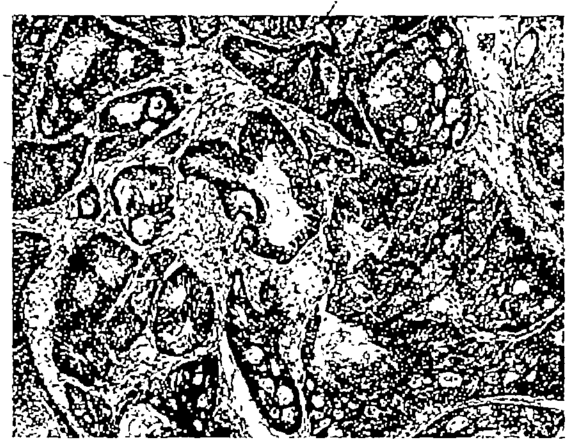


Fig. 2. *Case* 1. Histological section showing secondary adenocarcinoma of the penis.

Case 2: A 71-year-old male had an abdominoperineal excision of the rectum for carcinoma in May 1970. There were no secondary deposits at operation. The histology showed well-differentiated adenocarcinoma which had extended through the serosa and had involved the lymph nodes.

The patient made a good recovery and was well for 2½ years. until November 1972, when he developed pain in the perineal

---

* University Department of Surgery, University Hospital of Wales, Cardiff.

Table I: REVIEW OF CASES OF SECONDARY CARCINOMA OF THE PENIS FROM A RECTAL PRIMARY

Case no.	Author	Age (yr)	Symptoms	Physical findings	Treatment	Survival
1	Eberth (1870)	NS	NS	Infiltration of corpus cavernosum	NS	NS
2	Niewiesch (1933)	69	Priapism	Hard corpora cavernosa	Resection of bowel lesion, radical amputation of penis	10 mth
3	Matheson (1935)	72	Urinary retention	Nodules	Colostomy 1 mth earlier	5 mth after colostomy
4	Stein and Hautsch (1937)	62	Priapism diarrhoea	NS	Refused surgery	3 mth
5	Kerry and Gillies (1944)	60	Dysuria for 3 mth	NS	Amputation of penis	3 yr
6	Melicow and Ganem (1946)	NS	NS	Penile ulcer, inguinal adenopathy	Colostomy	2 mth
7	Thompson (1950)	70	Urinary retention with rectal pain	NS	Suprapubic cystoscopy +radiotherapy	4 mth
8	Cattell and Mace (1951)	30	Rectal bleeding for 9 mth, painful priapism	NS	Local excision	Alive and well 9 yr after surgery
9	Ney (1952)	NS	NS	Nodules in corpora	Colostomy, suprapubic	9 mth
10	Boyd (1954)	54	Noted several nodules	Nodules	Radical amputation	6 yr
11	Poutasse (1954)	72	Dysuria	Nodules in shaft of penis	None	6 mth
12	Poutasse (1954)	51	NS	Small nodule noted on shaft of penis	Amputation of penis	5 mth after amputation
13	Kaufman and Kaplan (1956)	47	Perineal pain	Hard nodule at right side of penile shaft	Perineal excision of tumour mass in cul-de-sac and prostate with X-ray of penis	4 mth
14	Whitelaw et al. (1956)	62	None	Ulcerative lesions on dorsum of glans penis 3–4 mm in diameter	Local excision of penile mass	2½ yr
15	Matt (1960)	48	Warts on penis		Local excision	3 mth
16	Tagart (1967)	75	Nodules on penis	Swelling of penis	Total penectomy	5 yr
17	Pond and Wade (1969)	64	Difficulty of micturition	Urethral meatus surrounded by tumour	Meatotomy	8 d
18	Poser and Kuttig (1972)	59	Retention of urine	Nodules on penis	Abdominoperineal excision of rectum. ? Excision of nodules	Alive after 2 yr
19	Selikowitz and Olson (1973)	48	Recurrent urinary retention	Nodular induration of corpora cavernosa, urethra and glans penis	Cystostomy	6 mth

NS, Not stated.

scar. A biopsy of the scar was performed and the histology showed adenocarcinoma compatible with an origin from the rectum.

After this procedure he developed acute retention of urine and required catheterization. In December 1972 a cystoscopy showed a hard shelf in the prostatic urethra and a trabeculated bladder. A transvesical prostatectomy with V resection of the bladder neck was performed. Histology of the bladder neck showed adenocarcinoma compatible with an origin from a primary large bowel tumour.

Three weeks later the perineal scar with the recurrence was widely excised. The tumour involved the perineal skin and bulbar urethra and extended deeply into the pelvis. The tumour was dissected from the urethra as far as the bulb of the penis but thereafter it was fixed and infiltrating. The perineum healed, but in April 1973 the patient again developed acute retention of urine. Urethroscopy showed a tight stenosis of the bulb which was solid with tumour and could only be dilated with difficulty. The patient was treated by a course of palliative radiotherapy to the pelvis with a marked improvement and spontaneously began to pass urine.

Four years after the abdominoperineal excision of rectum the patient is in good health and passes urine satisfactorily.

Discussion

The low frequency of occurrence of penile metastasis is surprising in view of the rich vascularity of the penis and its proximity to the rectum, bladder and prostate which are common sites of malignancy.

When penile metastases do occur they may present as either solitary or multiple nodules on the glans or in the body, or as solid infiltration of the corpus cavernosum, as in *Case* 2.

The previously reported cases of secondary carcinoma to the penis from a primary rectal carcinoma have been reviewed and the relevant data are shown in *Table I*. The symptoms reported include priapism, oedema of the penis, perineal pain and urinary retention. The urinary retention is probably due to compression and distortion of the urethra by secondary deposits. This view is shared by Selikowitz and Olsson (1973), who reported 2 cases of urinary retention due to urethral metastasis.

The methods of treatment have included local excision of metastasis, total penectomy, irradiation and the use of cytotoxic drugs. The number of cases is too small to state that any one method is superior to another.

It has been generally accepted that when secondaries have been identified the prognosis is poor, most patients being dead within 1 year. However, Cattell and Mace (1951), Boyd (1954) and Tagart (1967) have reported patients surviving 9, 6 and 5 years respectively after treatment of the penile metastasis. Two out of 3 of the long term survivors had radical amputation of the penis. The 2 cases described here are still alive 8 and 18 months after the penile metastasis appeared. They pose difficult management problems and perhaps a more aggressive attitude in the initial treatment of the penile metastasis, e.g. penectomy, would have improved the prognosis and made subsequent management easier.

The mechanisms of spread to the penis have been fully discussed by Paquin and Roland (1956); they include direct extension, spread by instrumentation, retrograde venous spread, direct arterial extension, retrograde lymphatic spread and paradoxical embolism. In the 2 cases reported here the most likely mechanism would appear to be direct extension since both patients had low rectal tumours and both had perineal recurrences. Stein and Hantsch (1937) considered that direct spread resulted from tumour extension into the corpus cavernosum via the ischiorectal fossa through the junction of the deep and superficial triangular ligament with Colles's fascia into the superficial perineal space.

Urinary retention occurring after abdominoperineal excision of the rectum is a well-recognized complication (Watson and Williams, 1952). The list of causes includes prostatic hyperplasia, autonomous neurogenic bladder, urethral stricture and postoperative malalignment of the bladder neck and urethra. The 2 cases reported emphasize that penile metastasis should be included in the differential diagnosis of urinary retention occurring after abdominoperineal excision of the rectum for carcinoma.

Acknowledgements

I wish to thank Mr G. Davies and Mr B. Peeling for permission to present their patients and also Mr P. Bolton for his advice.

References

ABESHOUSE B. S. and ABESHOUSE G. A. (1961) Metastatic tumours of the penis: a review of the literature and a report of two cases. *J. Urol.* **86**, 99–111.

BOYD H. L. (1954) Metastatic carcinoma secondary to carcinoma of the rectum: a review of the literature and report of a case. *J. Urol.* **71**, 82–90.

CATTELL R. B. and MACE A. J. (1951) Metastasis to the penis from a carcinoma of the rectum. *JAMA* **146**, 1230–1231.

EBERTH C. J. (1870) Krebsmetastasen des corpus cavernosum penis. *Virchows Arch. (Pathol. Anat.)* **51**, 145–146.

KAUFMAN J. J. and KAPLAN L. (1956) Secondary tumours of the penis. *Arch. Surg.* **73**, 105–111.

KERRY H. D. and GILLIES C. L. (1944) *The Urinary Tract: A Handbook of Roentgen Diagnosis.* Chicago, Yearbook Publishers, p. 298.

MATHESON N. M. (1935) Secondary carcinomatous deposits in body of penis with retention of urine. *Urol. Cutan. Rev.* **39**, 566–569.

MATT S. J. (1960) Metastatic carcinoma of penis secondary to adenocarcinoma of rectum: case report. *J. Urol.* **83**, 163–166.

MELICOW M. M. and GANEM E. J. (1946) Cancerous and precancerous lesions of the penis. *J. Urol.* **55**, 486–514.

NEY C. (1952) Secondary carcinoma of the penis arising from carcinoma of the rectum. *Arch. Surg.* **65**, 783–789.

NIEWIESCH M. (1933) Priapismus bei primaren und metastischen Geschwulsten in den Schellkovien des Penis. *Dtsch. Chir.* **241**, 94–98.

PAQUIN A. J. jun. and ROLAND S. I. (1956) Secondary carcinoma of the penis. *Cancer* **9**, 626–631.

POND H. S. and WADE J. C. (1969) Urinary obstruction secondary to metastatic carcinoma of the penis. *J. Urol.* **102**, 333–335.

POSER H. and KUTTIG J. (1972) Die Penis-Metastierung bei Adenokarzinom des Rektums. *Ther. Ggw.* **111**, 976–981.

POUTASSE E. F. (1954) Metastasis to the penis; report of four cases. *J. Urol.* **72**, 1196–1200.

SELIKOWITZ S. M. and OLSSON G. A. (1973) Metastatic urethral obstruction. *Arch. Surg.* **107**, 906–908.

STEIN J. J. and HANTSCH F. K. (1937) Adenocarcinoma of the rectum with unusual sites of metastasis. *JAMA* **108**, 1776–1778.

TAGART R. E. B. (1967) Secondary deposit of rectal carcinoma in the penis. *Proc. R. Soc. Med.* **60**, 501.

THOMPSON H. T. (1950) Involvement of the penis by a carcinoma of the rectum. *Surgery* **27**, 216–220.

WATSON P. C. and WILLIAMS D. I. (1952). The urological complications of excision of the rectum. *Br. J. Surg.* **40**, 19–28.

WHITELAW G. P., LEARD S. E., PARSONS L. and SHERWIN R. P. (1956) Carcinoma of the large bowel with metastasis to the genitalia. *Arch. Surg.* **73**, 171–178.

Br. J. Surg. Vol. 62 (1975) 80–84

Reviews and notices of books

Nontoxic Goiter. Concept and Controversy

Joel I. Hamburger, MD, FACP, Michigan. 235×160 mm. Pp. 222+x. Illustrated. 1973. Springfield, Ill.: Charles C. Thomas. $9.75.

This short book of about 200 pages which can be read in one or two evenings is a mine of practical information on the handling of thyroid disease excluding hyperthyroidism. It is written by a very busy practising thyroidologist who has already a similar book on hyperthroidism to his credit, published 5 years ago.

The book opens with a healthy critique of thyroid scanning, which puts it in its proper perspective, and then discusses non-toxic goitre, propounding the theory that if there is no goitre there is almost certainly no hypothyroidism. There is a review of thyroiditis, and then a good clinical approach to the problem of the thyroid nodule. The final six chapters are primarily concerned with thyroid cancer in all its aspects and it is interesting that the experience of the author is a little different from that in this country. Few would argue with his appraisal of the place of surgery and how far the operation should be extended. His experience of radioactive iodines has been on the whole rather disappointing, and his insistence on allowing the patient to develop hypothyroidism over 6 weeks, in order to obtain maximum uptake of isotope in the secondaries, is unkind to the patient though undoubtedly effective. His method of diuresis does not find many followers on this side of the Atlantic.

This is a very useful practical guide to the handling of patients with thyroid cancer and though didactic in presentation, the author is willing to support his line of action with good reason. As with all Thomas books the production is lavish and the price high by British standards.

SELWYN TAYLOR

Lectures on Methodology of Clinical Research

Max Hamilton, MD, FRCP, FRCPsych., FBPS, Wakefield. Second edition. 220×140 mm. Pp. 197+x. Illustrated. 1973. Edinburgh: Churchill Livingstone. £5.

Since Professor Hamilton's work deals with logic and the philosophy which should motivate and guide the aspiring research worker, that is how the lecture series start. Subsequent lectures deal with the nuts and bolts of statistical analysis, clearly explained and expounded. There is even a section on 'writing-up' and style, in which the prospective author is adjured to avoid popular and fashionable slang; what a pity that 'methodology' and 'experimentation' appear in the title and chapter headings—a bad example to the beginners but understandable since they are catchwords used in psychiatry and other subjects (or should one say 'disciplines'?) Nevertheless, this is a thoroughly readable and useful work which though written by a psychiatrist is applicable to any subject.

BRYAN N. BROOKE

Retinal Detachment. The Essentials of Management.

Hector B. Chawla, Chicago. 185×125 mm. Pp. 74. Illustrated. 1974. Edinburgh: Churchill Livingstone. £1·75.

It is difficult to know to whom this book is directed as an instruction in retinal detachment, while secondary detachment of the retina is virtually unmentioned. The short text contains many monochromatic drawings (understandably so because of the high expense of colour illustrations). Many surgeons would dispute the statements that retinal surgery should be carried out in specialist centres and that indirect ophthalmoscopy is the foremost basic skill—most surgeons would admit to the discovery of causal retinal tears with the aid of a direct ophthalmoscope which had been unnoticed by indirect ophthalmoscopy.

The text and illustrations leave much to be desired, being inadequate for the qualified surgeon and for the trainee about to prepare for higher examinations, although for a beginner in ophthalmology the book is a good introduction. Perhaps because of its brevity, the book leads the reader along too limited and selected channels of treatment, for example, the impression that air injection is therapeutically of paramount importance. There are many surgeons who repeatedly replace primary retinal detachments without the help of air. In the section on encircling bands the text leaves the reader completely ignorant on the correct positions and tension for tying the band, while it should be recognized that circumferential buckling at the equator does not necessarily produce retinal folds.

The section on anterior segment ischaemia seems to be too brief and, especially for the learner, contains insufficient information on its recognition and management.

Throughout, the book leaves too many questions and advocated therapeutic measures open for dispute, albeit that the treatment of retinal detachment is so varied. When planning future editions of this volume the author should seriously consider expanding the text to cover the subject more fully.

IAN M. DUGUID

Grundlagen der Nachsorge nach chirurgischen und urologischen Eingriffen

G. Jorns, Arnstadt, W. Remde, Potsdam, and H. Gerhard, Arnstadt. 220×155 mm. Pp. 280. Illustrated. 1974. Berlin: VEB Verlag Volk und Gesundheit. M.16.

This book on the fundamental principles concerning post-operative care covers a wide range of surgery. Somewhat surprisingly, cardiac surgery is discussed in one of the earlier chapters. The authors discuss postoperative management and the book is full of helpful advice even if basic physiological principles are scarcely mentioned. There are few illustrations and the appliances shown for the postoperative management of colostomies appear rather outdated by British standards.

The importance of rehabilitation in relation to an early return to work is stressed throughout.

H. B. ECKSTEIN

Therapeutic Aspects of Nutrition

Edited J. H. P. Jonxis, MD, H. K. A. Visser, MD, and J. A. Troelstra, MD. 230×160 mm. Pp. 344+xii. Illustrated. 1973. Leiden: H. E. Stenfert Kroese. 64P.

This excellent book contains the papers presented at the Fourth Nutritional Symposium held in Groningen in May 1973, and its rapid publication is most welcome. Whereas previous symposia have concentrated on the physiology and pathology of the newborn, the emphasis in this volume has shifted, with more discussion of nutritional principles and problems in the treatment of patients in hospital. There is still, however, a great deal of emphasis on the clinical difficulties of feeding the sick neonate and infant.

The book is divided into three sections which deal with physiological aspects of nutrition, the use of synthetic diets and parenteral nutrition respectively. The first section contains a series of authoritative but somewhat theoretical reviews of energy, water and salt requirements, protein, carbohydrates and linoleic acid as nutrients and some nutritional aspects of trace elements and vitamin D and E metabolism.

Of greater surgical interest is the second section, with a discussion of the use of elemental diets in the preoperative preparation of patients for abdominal surgery and in the management of malabsorption problems, intestinal fistulas and inflammatory bowel disease. The need to increase the elemental diet slowly for maximum benefit is stressed.

The third section is dominated by the care of the paediatric case, but it is suggested that supplementation of energy intake with 800 kcal/day of fat intravenously in adults can help with both energy balance and well-being and lead to an improvement in appetite. More practical details in this and the other sections would have been helpful but there is a great deal of interest in this review.

W. P. T. JAMES

Rontgenuntersuchung der Brust. Technik Diagnostik Differentialdiagnose Ergebnisse.
W. Hoeffken and M. Lanyi. 290 × 205 mm. Pp. 344 + viii, with 489 illustrations. 1973. Stuttgart: Georg Thieme Verlag. DM.148.

THIS book is devoted to radiological investigations of the breast. The first few chapters describe in detail the radiographic machinery required and the techniques used. The radiological appearances of the breast in specialized plain films, following contrast injection, and on arteriography are illustrated and compared with clinical photographs and, where relevant, with photomicrographs. It is clear that radiology of the breast has become a standard diagnostic technique. All conceivable pathological processes of the breast are discussed and described in relation to the radiological changes. Other methods of investigations such as thermography are detailed in an appendix.

The book is full of superb illustrations including many colour photographs of the clinical appearance of the breast which are invaluable for comparing with the radiographic appearance. There is no doubt that this book will become one of the standard volumes concerning radiology of the breast and it is undoubtedly of considerable interest to both radiologists and surgeons who specialize in treating diseases of the breast.

H. B. ECKSTEIN

The Management of Trauma
Edited Walter F. Ballinger II, MD, Robert B. Rutherford, MD, and George D. Zuidema, MD. Second edition. 250 × 175 mm. Pp. 795 + xiv, with 296 illustrations. 1973. London: W. B. Saunders Company. £12·40.

The most obvious difference between the first and second editions of *The Management of Trauma* is that the cover is now blue instead of green. In matters of detail there are a few spelling mistakes and the type face and headings are clearer. There are 20 fewer pages of text, and although the number of chapters is the same as before, radiation injuries, the role of the internist and psychological aspects have been omitted; vascular injuries have a chapter of their own and the management of fractures is covered in two chapters. A very useful chapter on mass disasters has been added.

Generally, the book has been brought well up to date; some chapters have been entirely rewritten and many others expanded or revised. The chapter on pathophysiology of trauma and shock contains a sound critical review of the work of Shires, and that on the treatment of shock is refreshing in its simplicity of approach, its invitation to look at the patient as well as records and for the fact that it refers to the work of Grant and Reeve and Ruscoe Clarke.

Renal failure and cardiopulmonary resuscitation and analgesia are described for surgical readers, but there is no mention of entonox in the latter chapter.

Injuries of the neck now include a section on the management of injuries of the large vessels in the neck. In the chapter on tracheostomy British readers will be surprised to find no mention of the Björk flap, and in the chapter on abdominal injury the experience of Ashton Miller and Mitchell with rupture of the urethra goes unrecorded. There is an unusually helpful account of the use and interpretation of plain radiographs of the injured belly.

There is much of practical value in this book but there is a curious variation from careful attention to detail, such as occurs in the section on wounds in the initial management of injuries of the lower limb, to a brief and general account, such as that of the injuries of nerves and tendons. There is, for example, now no mention of rupture of the tendo Achillis. The injured hand is dealt with in far too little detail to be of much assistance in matters of diagnosis and treatment, and it appears that news of the groin flap has yet to reach the United States. It seems also that orthopaedic surgeons have so far resisted invasion by A.O.

In summary, it is difficult to know for whom the editors intended this book; the quality is too uneven for it to satisfy the examination candidate on the one hand, or the perplexed surgeon confronted by a difficult case following injury on the other. One recognizes the immensity of the editors' task and the difficulty in striking a satisfactory balance between essentially practical guidance and comprehensiveness within a reasonable compass. Editors the world over will surely sympathize with the three men that have produced the two editions of this book. They have made quite striking changes and one may hope that in future editions there will be a more successful endeavour in pursuit of balance. Although the chapter on psychological aspects was not one of the most successful in the first edition it is a pity that the subject has been abandoned; perhaps this is because the title of the book refers only to trauma and not to those that suffer injury.

P. S. LONDON

Renal Histopathology. A Light Microscopy Study of Renal Disease
Robert Meadows, MD, FRCPA, Adelaide. 283 × 223 mm. Pp. 363 + xii. Illustrated. 1973. London: Oxford University Press. £14.

THIS book describes the morphological changes of renal disease as seen with the light microscope, drawing upon the newer techniques of immunofluorescence and electron microscopy only in so far as they help to elucidate light microscopic appearances. It concentrates mainly on renal biopsy material, the approach to which is dealt with admirably in the preface, and includes a useful chapter on technique to help the reader gain the maximum information possible from the material available.

The book is in two parts. Part 1 describes the individual structures of which the kidney is composed and their response to various disease processes. Part 2 deals with specific diseases as they affect the kidney as a whole. This approach inevitably leads to some repetition but is of value in stressing the importance of systematic assessment in building up a composite picture of the pathological changes present before considering diagnosis. One disadvantage is that, when using the book for reference purposes, more than one chapter may have to be consulted to cover a single subject.

The author's personal experience and the literature on the subject are well integrated and the illustrations are numerous and very adequate. Of special value is the use of serial biopsies in the individual patient to trace the natural course of a disease or to study the modifications due to therapy.

On some subjects detail is lacking. For example, the later stages of idiopathic membranous glomerulonephritis are not described. Nevertheless, the book is fairly comprehensive and can be recommended to both histopathologists and renal physicians.

KATHERINE M. CAMERON

Basic Clinical Surgery for Nurses and Medical Students
Edited John McFarland, Liverpool. 222 × 140 mm. Pp. 767 + xviii. Illustrated. 1973. London: The Butterworth Group. £2·20.

THE idea of a book on basic clinical surgery being suitable for nurses and medical students is at first difficult to accept. One instinctively suspects that it would contain too much for the nurse and too little for the medical student. From the nursing point of view there is an excellent all-round cover of the subject, the inclusion of a chapter on the care of children with congenital disorders being particularly welcome. Details of investigations and patient care not generally included in surgical nursing books are invaluable. The sketch diagrams are excellent, making it an ideal quick reference book, useful for all grades of students and trained nursing staff. From the point of view of the medical student starting his clinical work it provides a useful introduction and practical guide but it is not enough for his final examinations. It is well produced, clearly written and wastes no words.

IAN MCCOLL

Reviews and notices of books

Orthopaedic Surgery and Traumatology

Edited R. De Marneffe and E. Vander Elst. 245 × 175 mm. Pp. 1155+xxiv. Illustrated. 1974. Amsterdam: Elsevier Excerpta Medica North Holland. D.Fl. 275.

ONLY to translate, collate and edit more than 400 papers in half a dozen languages is a considerable achievement. To have done so in such a way as to make the material readily available and the whole book eminently readable is a truly remarkable editorial feat.

The book comprises the proceedings of the Twelfth Congress of the International Society for Orthopaedic Surgery and Traumatology (SICOT) which was held in Tel Aviv in October 1972, and there is to be found in its 1200 pages some reference to every item of interest to contemporary orthopaedic surgeons. To achieve the objective of such a report, very careful indexing and cross-reference is essential and this has been neatly and adequately achieved. It is interesting to read how global are the problems which confront orthopaedic and accident surgeons, and fascinating to catch a glimpse of the thought and practice of surgeons far afield and how they deal with the problems which confront all of us. Important sections will be found on artificial joint replacement and malignant tumours of bone, and of subjects so diverse as, for example, the use of Chymopapain in the treatment of lumbar disk disease, spondylolisthesis, haemostatic deficiency surgery—the list is endless.

All those engaged in the surgery, clinical investigation or laboratory research of disease affecting the locomotor system are well advised to have this volume for easy reference on the library shelf. The book cannot, of course, be read through from cover to cover, nor is it intended to be. Like a good dictionary it will undoubtedly find episodic and invaluable use. The quality of paper, print and illustrations is faultless. A monumental editorial task has been brilliantly achieved.

L. KESSEL

The Surgery of the Central Nervous System

D. W. C. Northfield, MS, FRCS, FRCP, London. 254 × 205 mm. Pp. 884+xi. Illustrated. 1973. Oxford: Blackwell Scientific Publications. £22·50.

MR NORTHFIELD is a link, and a very lively one, between present day neurological surgery and the founders of the subject in this country almost 50 years ago. His experience is vast and his knowledge of both the practical and academic aspects of the subject is unrivalled. All of us, in particular those in training, owe him a great debt for the care and industry that have gone into the production of this account of neurological surgery. At a time when multiple authorship is almost obligatory, this beautifully produced volume must be unique. It has the great virtue of presenting a fair cross-section of informed opinion on any subject with the author's assessment based on his personal experience. It is comprehensive and authoritative with an excellent and apparently very accurate bibliography. The style is easy and, although it may not be everyone's idea of a bedside book, it is no exaggeration to say that it can be read for pleasure. I am in no doubt that it is by far the best available book on the subject in English, providing as it does a bridge between what textbooks there are and the scientific literature. A wider audience than that provided by neurosurgeons can be confidently expected amongst medical neurologists and physicians and surgeons to whom it can be recommended without reservation.

The relevant clinical neurology, histology and neuroradiological techniques are dealt with in detail, but wisely the author has refrained from an attempt to include details of operative technique. This does not mean that he does not express opinions on the type and scope of surgical procedures or the likely results of surgery, but he takes the view that technique is taught by apprenticeship and this restraint has limited to some extent the size and expense of the volume which, nevertheless, are still not inconsiderable. This book will prove a necessary addition to personal and departmental libraries.

JOHN HANKINSON

Current Practice in Orthopaedic Surgery. Volume 5, 1973

Edited James P. Ahstrom Jun., MD, Illinois. 255 × 180 mm. Pp. 308+ix. Illustrated. 1973. London: Henry Kimpton. £13·25.

IN this, the fifth annual volume of brief monographs on orthopaedic subjects of topical interest, much depends on the subject selected and the man to write it. Both choices by the editor have here been usually excellent though inevitably patchy.

The 'Management of Low Back Pain' by Ian McNab of Toronto is a superb short account of this problem. McNab has contributed much new knowledge to this field. However, his greatest contribution in this article is his succinct and beautifully clear and descriptive account of a complex problem. All who read this will learn.

'Arthroscopy of the Knee' by Robert Jackson of Toronto is a good survey of this new technique with some consideration of its advantages and limitations.

There are three contributions to the subject of total joint replacement, obviously an important and rapidly changing technical problem. All three are well worth reading.

Samilson has made some interesting observations on scoliosis in cerebral palsy, until now a neglected subject. DeWald reviews 'New Trends in the Operative Treatment of Scoliosis', an area of surgery undergoing dramatic changes with the new technical advances of the past decade or two. It is perhaps a rather dry matter-of-fact account with too little comment on the special indications and difficulties of the alternative methods.

There are in all eleven contributions, and the reviewer found all worth reading and a few outstanding.

J. I. P. JAMES

Recent Advances in Thrombosis

Edited L. Poller, Manchester. 212 × 146 mm. Pp. 227+ix. Illustrated. 1973. Edinburgh: Churchill Livingstone. £5·50.

TEN papers, seven from Europe and three from the USA, have been collected from those of eleven simultaneous sessions at the 1972 Congress of the International Society on Thrombosis and Haemostasis; the editorial policy was to choose from areas of active investigation. Personal distinction on the part of the contributors could well have been another factor in the selection, for the list includes many household names in this growing discipline. The fact that much of the material presented is more of a progress report than on new work in no way lessens its value. As a guide to the present state of knowledge, and the paths by which this has been reached, it cannot be faulted. The literature is presented with a wise and critical selectivity, and the reference value of the book is much helped by the excellent index. Among the many stimulating sections a few choose themselves for special mention: for example, Sevitt on the morbid anatomy of sites of origin, Vessey on the modern trend in epidemiology, Vermylen and colleagues on the role of the platelets, including the effect of aspirin and other active drugs, Prentice and McNicol on treatment by fibrinolysis and the editor himself on the effects of the contraceptive pill. Other chapters of equal merit make up a most interesting and valuable compact source of good reading and useful reference.

H. H. G. EASTCOTT

Tumors of the Extra-adrenal Paraganglion System (including Chemoreceptors)

George G. Glenner, MD, and Philip M. Grimley, MD, Maryland. 260 × 200 mm. Pp. 90. Illustrated. 1974. Washington: Armed Forces Institute of Pathology. $4·50.

THIS book is the latest addition to the well-known and authoritative *Atlas of Tumor Pathology*. Although written primarily for pathologists, it will be of value to surgeons who encounter any of the rare paraganglionic tumours. In addition to the excellent pathological descriptions, it contains a clear and concise account of the anatomical distribution, clinical features, differential diagnosis, endocrine activity and treatment of the paraganglionic tumours.

R. B. WELBOURN

Care of the Ostomy Patient

Virginia C. Vukovich, RNET, and Reba D. Grubb, Arizona. 227×150 mm. Pp. 138+xii, with 23 illustrations. 1973. London: Henry Kimpton. £2·35.

THE aims of this book are highly commendable. The increasing interest in the total care, support and rehabilitation of the ostomy patient is long overdue, and those concerned with these people should make every effort to spread this concept. The psychological trauma of facing up to a situation in which faeces are discharged on to the abdomen is great in itself, without the associated problems such as odour, leaking appliances and sore skin with which this group of people has to contend. Until quite recently the attitude has been that this is something that the patients must learn to live with! Any book, therefore, that promotes interest in this subject can only do good, and this one, in particular, is well planned, researched and written.

It covers the medical aspects for the reasons for creating a stoma and its practical care and management; also suggested educational programmes for teaching both experienced nurses and non-professionals who are interested in giving some service, supportive and practical, for these patients.

The section on practical management is clear and comprehensive; obviously there are differing opinions on specific treatments, such as using solvents on the skin, but anyone studying this book could learn some good principles.

The advice on counselling the patient before operation is especially good; this is sadly lacking still in many hospitals in this country and elsewhere, but is the most important step in helping the patient in the process of acceptance and rehabilitation.

On the educational side, the training programmes described may be suitable for the United States but the reviewer feels that they are not really geared to the needs of nurses in Britain. With smaller financial resources available these programmes tend to be more concentrated. If our own students are taught the necessity for giving support and information to these patients, and the basic problems and management of the stoma are understood, by involving them in as much active practical experience as possible during a course, combined with good lectures and discussions related to the subject, this should be sufficient.

In all, this book would be a welcome addition to any library used by people concerned with this group of patients.

BARBARA SAUNDERS

A History of the Army Medical Department. Volumes 1 and 2.

Lt-Gen. Sir Neil Cantlie, Late Director General, Army Medical Service. 240×160 mm. Volume 1: Pp. 519. Volume 2: Pp. 448. Illustrated. 1974. Edinburgh: Churchill Livingstone. £12.

THE traditions of our Medical Corps have always inspired pride. These feelings have been enhanced by this comprehensive, detailed and fascinating record of all that led up to and contributed to its formation, step by step. Progress continued in spite of the almost overwhelming military prejudice and ignorance.

Volume 1 (1660–1853) and Volume 2 (1854–1898) are meticulously supported by full lists of references. These volumes, especially Volume 2, should be of great interest to all surgeons and others concerned with the care of the sick and wounded. The author, with his experience as a surgeon and as a Director General of the Army Medical Service, proves his talents and quality as a critic, historian and writer. He held the reviewer's interest throughout, in spite of many repetitions in the first volume. To condense this very complete record to one volume would have sacrificed much of great value. Statistics and uninspiring reports are interspersed and enlivened by masterly descriptions of conditions and pen pictures of events vividly recorded by participants at the time. This is highlighted by the citations of the Victoria Crosses awarded.

Throughout this history the same military administrative, medical and surgical mistakes are repeated over and over again. With this readily accessible record, collected together in one place, along with authentic and interesting details unearthed from the past, they should not be repeated. Had the reviewer read this before the Second World War he would have been much wiser.

Useful guidelines for fighting future administrative battles, with strong support as in the past from civilian colleagues in the Royal Colleges and the BMA, will be found in these volumes. The blood of warriors has trained many surgeons.

R. A. STEPHEN

Chirurgie der Gegenwart. Volume 5

Edited Rudolf Zenker, München, Franz Deucher, Aarau, and Wilhelm Schink, Köln. 260×180 mm. Pp. 121. Illustrated. 1974. München: Urban & Schwarzenberg. No price given.

THIS is the orthopaedic volume of the new loose-leaf textbook of surgery. Apart from a large and relatively empty folder it includes the first 7 chapters. The first chapter by Professor Mau attempts to deal with all congenital abnormalities of the skeletal system, and the illustrations certainly suggest that the corrections of such abnormalities require a vast amount of ironmongery. The second chapter deals with the diseases of joints, while the third chapter is academic and discusses the development of arthritis. Other chapters deal with rheumatic disease, diseases of the intervertebral discs and all sinovial membranes.

It is noteworthy that some of the references quoted are as recent as 1973.

H. B. ECKSTEIN

1972 Surgery Annual. Volume 4

Edited Philip Cooper, New York, and Lloyd M. Nyhus, Illinois, 235×172 mm. Pp. 445+ix. Illustrated. 1972. New York; Appleton-Century-Crofts. $19.25.

A VARIED and variable volume. There is an excellent review on shock, but the treatment of venous thrombo-embolism contains no references to the excellent contributions from the United Kingdom in the past few years. The chapter on peptic ulcer illustrates closure of the duodenum in several diagrams, as well as photographs, which seems unnecessary in this kind of book. Curiously, the references on follow-up after vagotomy omit the papers by Goligher and his colleagues. Chapters on the short gut syndrome and the significance of ileal resection are complementary and well written, but elsewhere the book is less thorough and the references are sometimes limited and inadequate.

This book is for the library, and most British surgeons will consult it there.

C. G. CLARK

Klinische Urologie. Ein Lehrbuch.

Edited C. E. Alken and W. Staehler. 265×180 mm. Pp. 611+xvi. Illustrated. 1973. Stuttgart: Georg Thieme Verlag. DM.148.

THIS is a new textbook of urology in which 32 leading urologists and others from Germany, Austria and Switzerland have collaborated. Alken's introductory chapter stressing the need for expansion of urology in Germany should provide useful information for the British Association of Urological Surgeons! Every conceivable aspect of urology is covered and the book includes chapters on urology in the female, renal hypertension and renal failure. There is even a chapter on the assessment of disability in relation to urinary tract disease and a rather fascinating summary of the history relating to urology going back to 2000 B.C. Paediatric urology has been covered extensively by R. Hohenfellner and his colleagues.

The volume is illustrated throughout by excellent reproductions of radiographs, some very good line diagrams and 3 pages of well-reproduced colour illustrations. As each chapter has been written by an authority on the subject, it is perhaps reasonable that the references quoted are minimal and are largely restricted to the German literature.

The volume is beautifully produced and completely up to date and should be of considerable interest to any urologist who can understand German.

H. B. ECKSTEIN

Book notices

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

Hyperparathyroidism

Edward Paloyan, MD, Illinois, Ann M. Lawrence, MD, Illinois and Francis H. Straus, MD, Illinois. 233×158 mm. Pp. 222+x. Illustrated. 1973. New York: Grune & Stratton Inc. $16.00.

Mammography, Thermography and Ultrasonography in Breast Disease (Radiology in Clinical Diagnosis Series)

K. T. Evans and I. H. Gravelle. 210×127 mm. Pp. 148+x. Illustrated. 1973. London: Butterworths. £4·45.

Anaesthesiology and Resuscitation. Ketamin.

R. Frey, Mainz, F. Kern, St Gallen, and O. Mayrhofer, Wien. 229×152 mm. Pp. 464+xv. Illustrated. 1972. New York: Springer-Verlag. $25.20.

Anaesthetics, Resuscitation and Intensive Care

W. Norris, Glasgow, and D. Campbell, Glasgow. Fourth edition. 250×140 mm. Pp. 289+xii. Illustrated. 1974. Edinburgh: Churchill Livingstone. £2.

The Nature of Cancer. Volume 1.

Manu Kothari and Lopa Mehta. 245×185 mm. Pp. 902+xxx, with 132 illustrations. 1973. Bombay: Kothari Medical Publications. £12.

A Companion to Surgical Studies

R. Nigam, New Delhi. 240×170 mm. Pp. 623. Illustrated. 1973. New Delhi: Academic Books Limited. Rs.22.

Uveitis, Immunologic and Allergic Phenomena

R. Campinchi et al. Translated, revised and indexed by Bruce Golden, Johannesburg, and Marlette M. Givioset, Iowa. 254×171mm. Pp. 818+xvi. 1973. Springfield, Ill.: Charles C. Thomas. $39.50.

DuVries' Surgery of the Foot

Verne T. Inman, San Francisco. Third edition. 260×184 mm. Pp. 567+xvi. 1973. London: Henry Kimpton. £12·35.

1973 Pathology Annual

Series editor, Sheldon C. Sommers, New York. 241×171 mm. Pp. 479+viii. 1973. New York: Appleton-Century-Crofts. $18.50.

Biomedical Materials Symposium No. 4. Materials and Design Considerations for the Attachment of Prostheses to the Musculoskeletal System.

Edited S. F. Hulbert, S. N. Levine and D. D. Moyle, South Carolina. 235×152 mm. Pp. 465+xii. 1973. Chichester: John Wiley & Sons Ltd. £9.

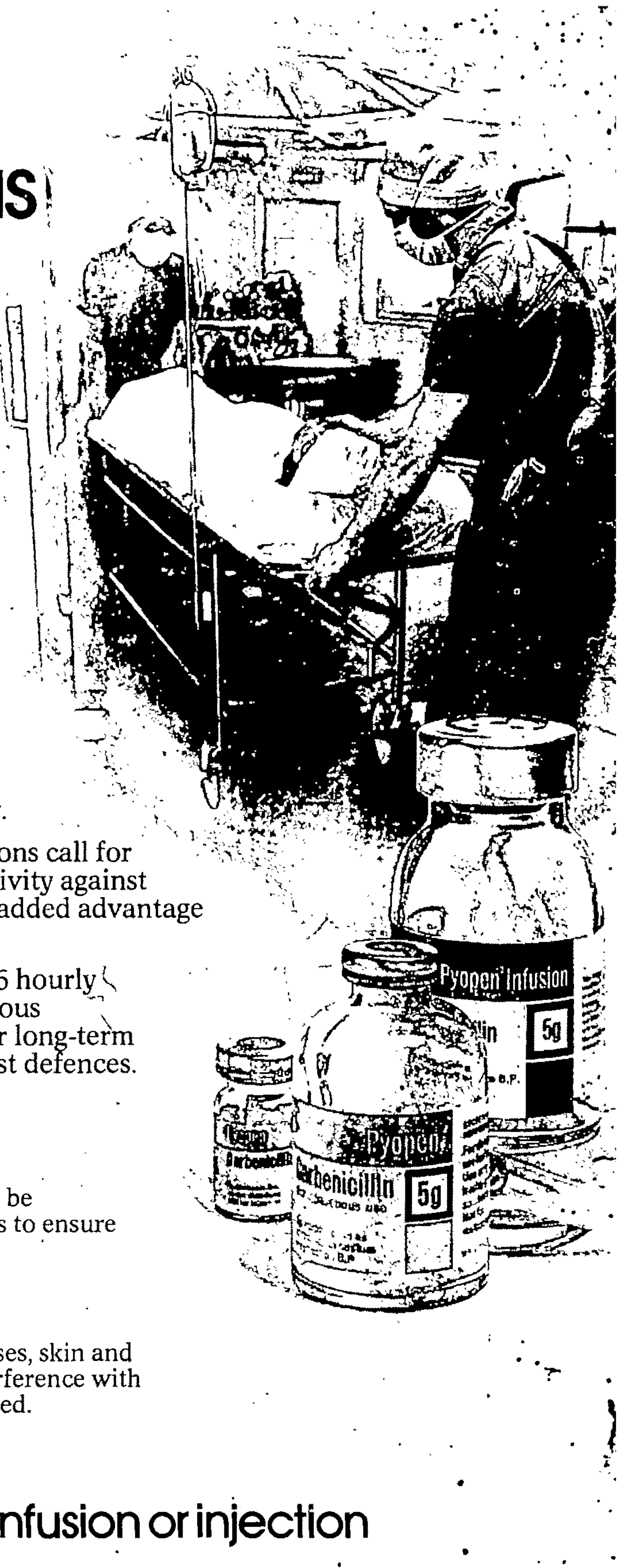
Physician's Handbook

Edited Marcus Krupp et al., California. Seventeenth edition. 178×108 mm. Pp. 727. 1973. California: Lange Medical Publications. $6.50.

A System of Orthopaedics and Fractures

A. Graham Apley. 206×178 mm. Pp. 540+x. 1973. London: The Butterworth Group. £8·80.

When pseudomonas threatens...



Pyopen

The skill of the surgical team, hours in the theatre, the most advanced techniques in the world . . . and infection can still throw the outcome into jeopardy.

Systemic pseudomonas or proteus infections call for Pyopen. Only Pyopen offers you good activity against these Gram-negative organisms with the added advantage of penicillin safety.

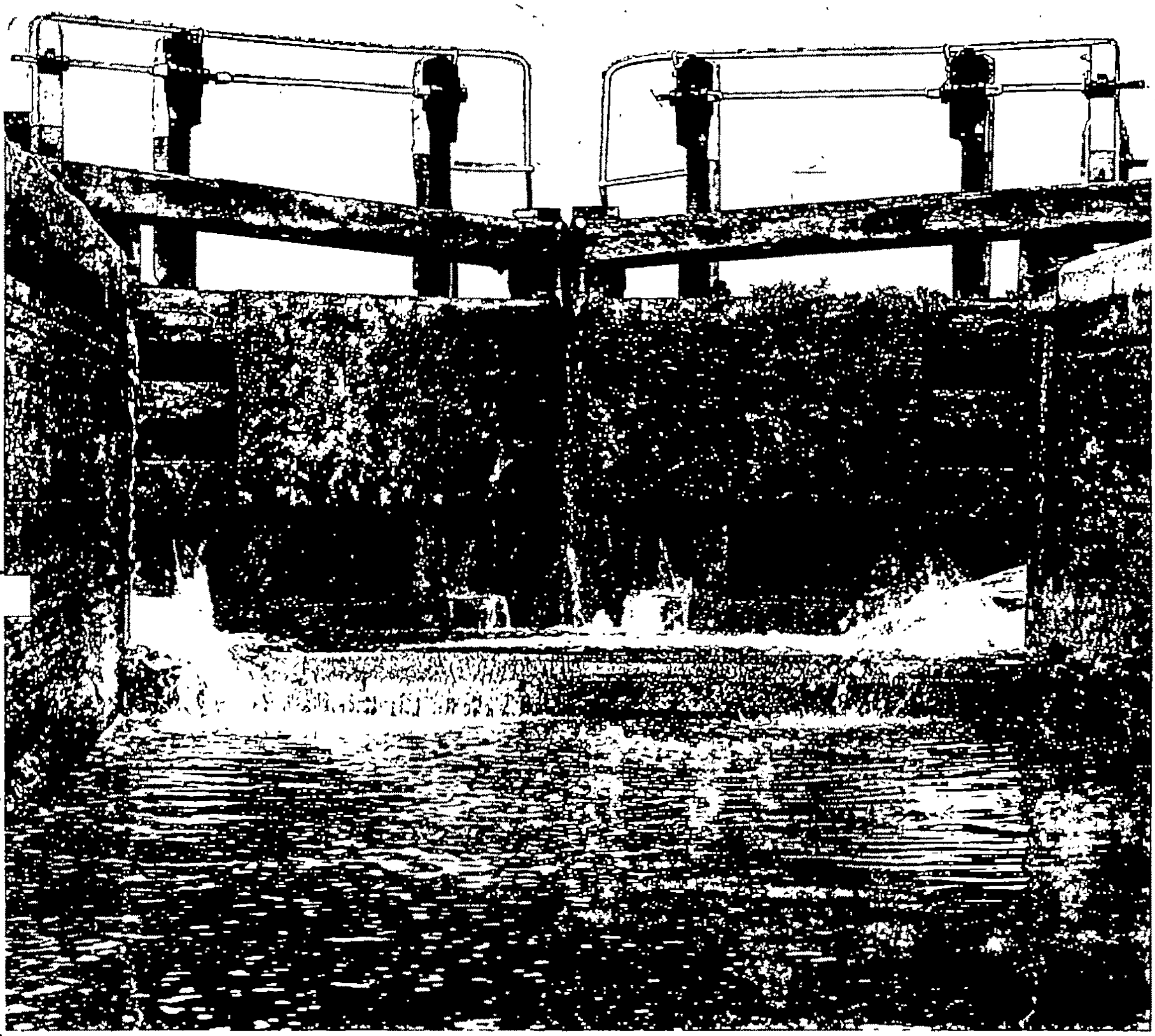
Intravenous Pyopen, at a dosage of 5g 4–6 hourly will rapidly control many of these dangerous infections. And Pyopen is also suitable for long-term therapy and for patients with lowered host defences.

Adult Dosage
5g I.V. 4–6 hourly.
In patients with renal impairment dosage may be reduced; monitoring is advisable in these cases to ensure adequate serum antibiotic levels.
Contra-indication
Penicillin hypersensitivity.
Side-effects
As with other injectable penicillins. In rare cases, skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Pyopen - by infusion or injection

Further information is available on request.
Pyopen* (carbenicillin sodium B.P.) is a British product originated by
Beecham Research Laboratories, Brentford, England. *regd.

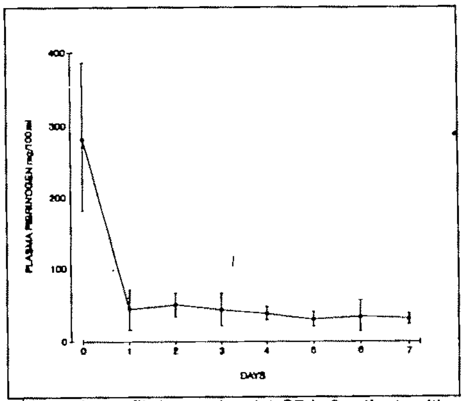
A new concept in the control of occlusive vascular disease



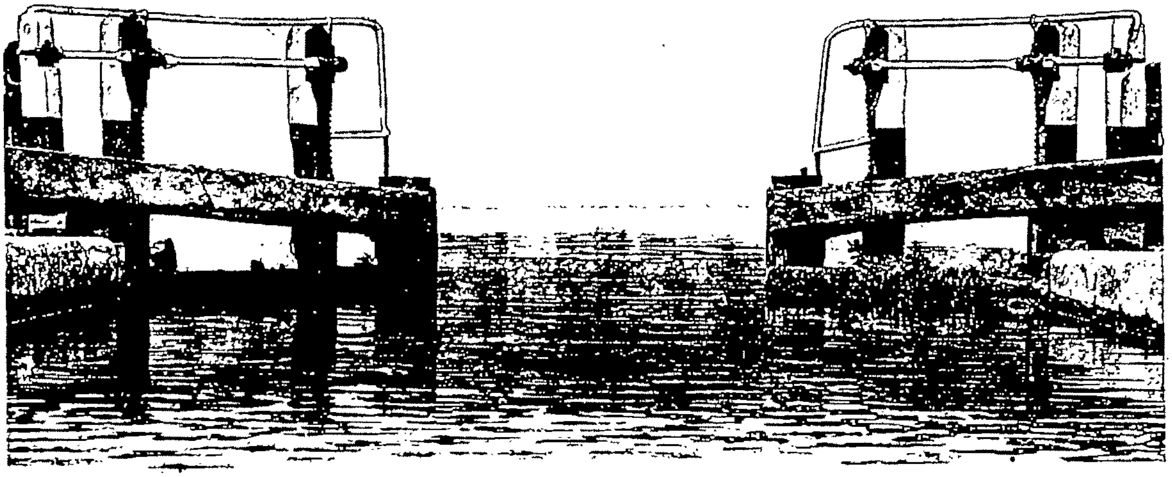
A unique drug is now available to the specialist for routine anticoagulant therapy, and to the researcher as an aid to the elucidation of thromboembolic disorders. Its name is Arvin.

Arvin reduces plasma fibrinogen to a level that maintains marked hypocoagulability without serious spontaneous bleeding complications. This desirable effect is achieved through the specificity of Arvin for fibrinogen—other clotting factors are unaffected.

This state of 'pure' defibrination has an important clinical place when prophylactic measures need to be taken in occlusive vascular disease, e.g. to prevent the formation and extension of thrombi and the dissemination of emboli.



Mean plasma fibrinogen level ± SD in 9 patients with venous thromboses. Arvin 2 units/kg body weight intravenously every 12 hours. From Pitney WR, (1971). Thromb Diath Haemorrh, *45*, 43.



Consistent features of Arvin therapy include an absence of thromboembolic events during treatment, absence of fibrinogen rebound and low incidence of rethrombosis after treatment has ceased. On withdrawal, plasma fibrinogen returns to haemostatic levels within 12 hours and to normal after 10-20 days. Thus, the changeover to oral anticoagulants is smooth and complication-free.

A consistent dose-effect relationship which ensures simple and precise control methods has been established for Arvin. On this basis, we can recommend this drug for a range of indications where controlled therapeutic defibrination is desirable.

For instance, deep vein thromboses, central retinal and branch vein thrombosis, priapism, pulmonary hypertension of embolic origin, embolism after prosthetic cardiac surgery and rethrombosis after thrombolytic therapy have been shown in clinical trials to respond well to Arvin.

To find out more about the unique Arvin concept specialists are invited to write to us for detailed clinical literature and prescribing information.

Arvin
ancrod
controlled therapeutic defibrination

J4501

Berk Pharmaceuticals. Shalford, Surrey.

Arvin is a registered trademark.

Nolvadex–a more acceptable approach to breast cancer treatment

Drug therapy is often both uncomfortable and distressing for the patient with advanced breast cancer. But now a more acceptable treatment is available for such patients, 'Nolvadex' (tamoxifen).

'Nolvadex' is an oestrogen antagonist. Whilst it is just as effective as other treatments, it has no hormonal properties. Virilization–common with androgens–is unknown; oedema, nausea and vomiting occur much less frequently than with oestrogens.

'Nolvadex' is taken as twice-daily oral doses. So treatment is simple as well as more acceptable.

Further information–including the results of U.K. trials with 'Nolvadex'[1,2] is available on request.
References: 1 *British Journal of Cancer* (1971), 25, 270.
2 *British Medical Journal* (1973), 1, 13.

Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

Nolvadex
Easier to give, easier to take

'Nolvadex' is a trade mark

PH

Fight cancer with a will

When testators ask your advice, please remind them of the urgent work of the Imperial Cancer Research Fund. In the Fund's up-to-date laboratories trained minds are using every weapon of modern science to fight all forms of cancer, including leukaemia.

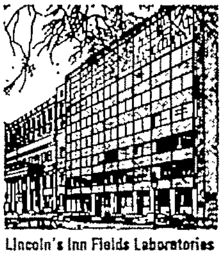
Now one of the world's great research centres, the I.C.R.F. relies entirely on public support. The cancer problem *must* be solved. Please help now.

Patron:
H.M. THE QUEEN
President:
The Honourable Angus Ogilvy

Form of Bequest

I hereby bequeath the sum of..................pounds free of duty to the Imperial Cancer Research Fund, Lincoln's Inn Fields, London, WC2A 3PX for the purpose of scientific research, and I direct that the receipt of the Honorary Treasurer or Secretary shall be a good discharge for such legacy.

Please write for further information to: The Secretary, I.C.R.F. (Dept 164), PO Box 123, Lincoln's Inn Fields, London WC2A 3PX



Lincoln's Inn Fields Laboratories

IMPERIAL CANCER RESEARCH FUND

H. K. Lewis & Co. Ltd.

Medical Publishers
and Booksellers

136 GOWER STREET
LONDON, WC1E 6BS

Telephone : 01-387 4282

LEWIS'S
MEDICAL LIBRARY

Annual Subscription from £3·00

Books may be exchanged as often as desired. There are reduced rates for multiple subscriptions.

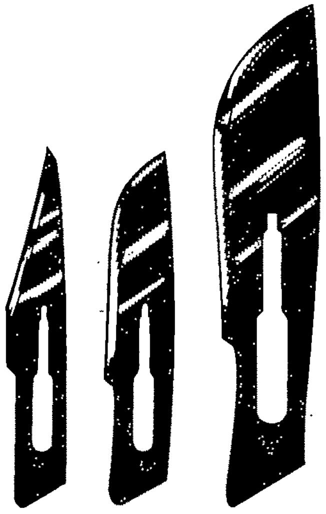
Prospectus post free on request

The operative word is

Swann-Morton

surgical blades

SWANN-MORTON LIMITED, PENN WORKS,
OWLERTON GREEN, SHEFFIELD S6 2BJ, ENGLAND.



BURNS including Thermal Injury

The Journal of the International Society for Burn Injuries

Editor: J. E. LAING, FRCS

Published Quarterly Annual Subscription £8·50 (post free) Single Copies £2·40 (post free)

JOHN WRIGHT 42-44 Triangle West
Bristol BS8 1EX

The single solution

for parenteral nutrition

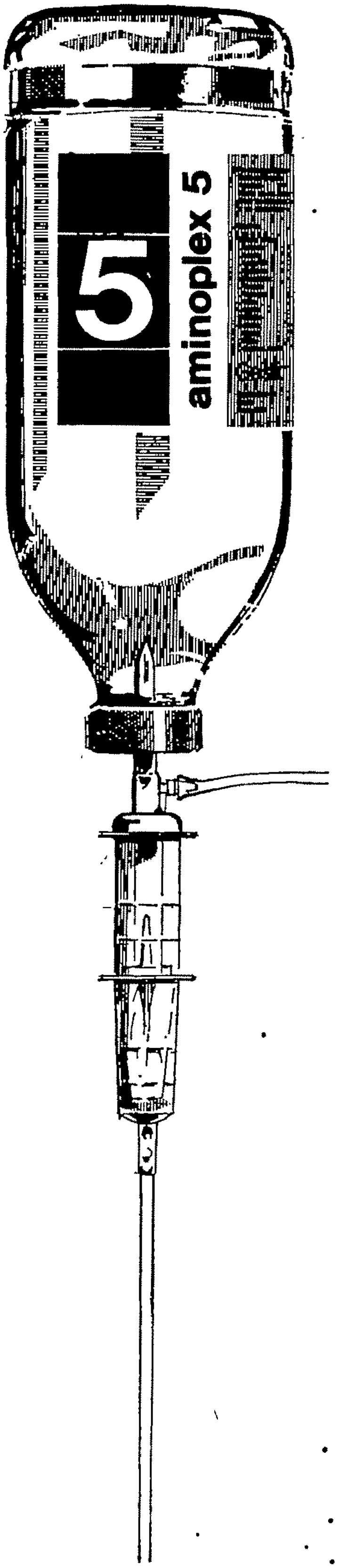
Aminoplex 5

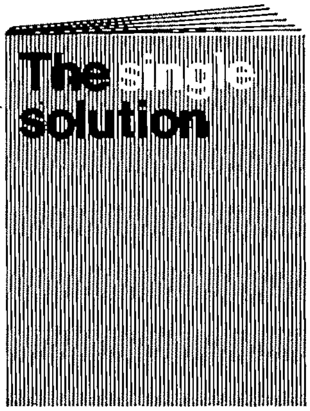
1 litre three times per day
provides 15g. of utilisable
nitrogen and 3000K calories;
the nutrient content being
derived from synthetic
L-Form amino acids,
sorbitol and alcohol.

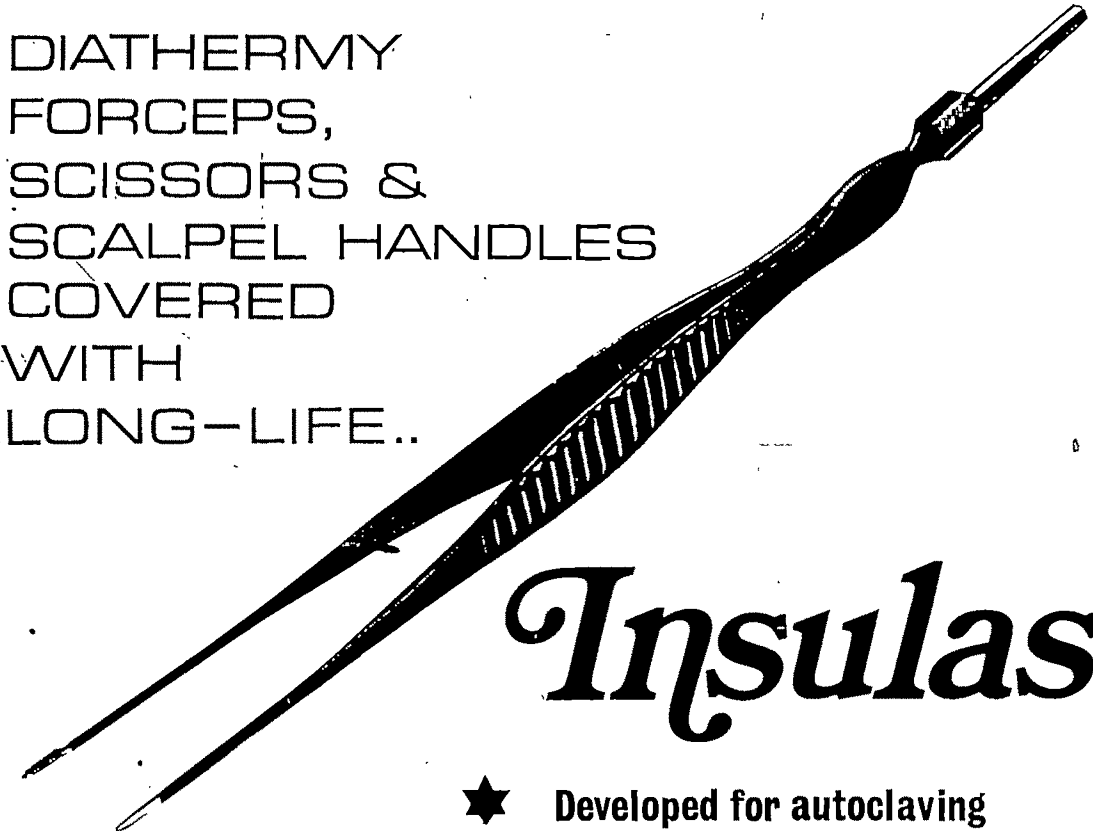
Geistlich
Chester

In co-operation with Salvia-Werk
G.m.b.H., Homburg/Saar, W.Germany.

Medical literature
available from:
Geistlich Sons Ltd.,
Newton Bank,
Long Lane,
Chester CH2 3QZ.
Telephone
Chester 47534-7







GU

NEW

DIATHERMY
FORCEPS,
SCISSORS &
SCALPEL HANDLES
COVERED
WITH
.LONG-LIFE..

Insulast

- ✶ Developed for autoclaving
- ✶ ECONOMICAL · saves on repairs
- ✶ SAFER · crack resistant
- ✶ THINNER · better grip
- ✶ Universal cable fitting

When ordering new diathermy instruments, or requiring old instruments to be re-insulated, always specify 'INSULAST' only obtainable from;

The G.U. Manufacturing Co. Ltd.

28a, Devonshire Street, London, W1N 2AJ
Telephone; 01-935-2835.

Why run the risk of her cystitis ascending, and the problem of pyelonephritis developing? Rapid, effective therapy with SEPTRIN is indicated at the first opportunity.

SEPTRIN was rated top oral treatment in a British survey of 23,491 urinary pathogen sensitivities.[1] SEPTRIN has been judged superior to ampicillin[2,3] and is now well established as a first-line treatment for urinary infections.

SEPTRIN contains trimethoprim and sulphamethoxazole, Full prescribing information is available on request.

Wellcome

1 *Postgrad med J.* (1971) **47**. Supplement (September), 7.
2 *Brit med J.* (1972) **2**, 673.
3 *Clin Trials J.* (1972) **9/3**, 9

Wellcome Medical Division
The Wellcome Foundation Ltd.
Berkhamsted, Herts

SEPTRIN

TRADE MARK

Sodium Fusidate

fucidin®

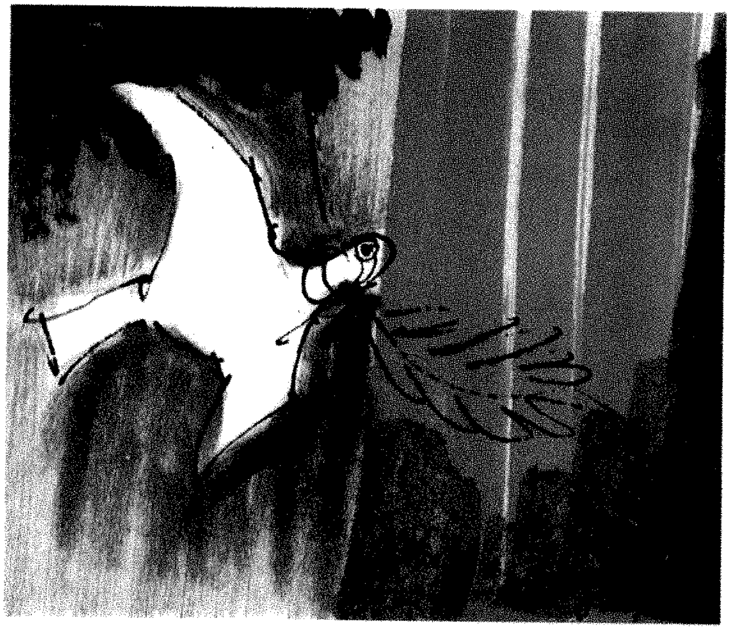
Now the orthodox treatment for staphylococcal infections

- ✻ Journal of Bone and Joint Surgery, 1972 (May).
- ✻ British Medical Journal, leading article, Volume 1, page 126, 1970.
- ✻ Journal of Bone and Joint Surgery, Volume 52B, No. 2. 1970.
- ✻ Quarterly Journal of Medicine, Volume 38, No. 149, 1969.
- ✻ British Journal of Clinical Practice, Volume 23, No. 1., 1969.
- ✻ British Medical Journal, leading article, Volume 4, page 656, 1968.

and more than 160 other original publications

Further information available on request
LEO LABORATORIES LIMITED
L E O HAYES MIDDLESEX Tel: 01-573 6224

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU



"I Bring Peace"-73

"It is concluded that maintenance treatment of ulcerative colitis with sulphasalazine (salazopyrin) should be continued indefinitely unless contraindicated by side effects".[1]

The results of the above controlled trial carried out at the Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford are all the more welcome as earlier trials of cortisone[2] and prednisone[3] at standard dosages have shown them to be ineffective in reducing the number of recurrences of ulcerative colitis.

"Fortunately, Sulphasalazine tablets, 0.5 grams 4 times a day will prevent relapses in the majority of patients with colitis, and only a few patients cannot tolerate this relatively small dose, which can be continued indefinitely since we do not know when, if ever, it can be safely stopped".[4]

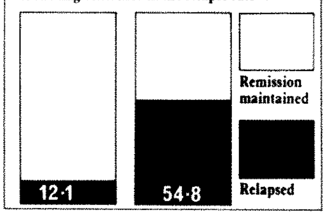
Salazopyrin (sulphasalazine) is available as the plain 0.5g. tablet, 0.5g. EN-tab and as an 0.5g. suppository. Literature and detailed information on Salazopyrin are available on request.

Salazopyrin is a registered trade mark.

Salazopyrin

– to be continued indefinitely

"A striking difference in the relapse rate".



"The patients who received dummy tablets had more than four times the relapse rate of those receiving sulphasalazine".[1] (Salazopyrin).

"Both groups of patients had been satisfactorily maintained for 1 – 5 years on Salazopyrin prior to the study, in which they took Salazopyrin or placebo for 6 months."

References
1. Gut (1973) *14* 923 – 926
2. Brit. med. J. (1959) *1* 387 – 394
3. Lancet (1965) *i* 188 – 189
4. General Practitioner (1972) April 7 p11

Further information on request from:–
Pharmacia (Great Britain) Ltd.
Paramount House,
75 Uxbridge Road,
London W5 5SS.
Telephone: 01-579 0102/7

Pharmacia

Vol. 62 : No. 2 : February 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society)
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
*SIR IAN MCADAM Kampala : Uganda
A. C. MCEACHERN Adelaide : Australia

W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

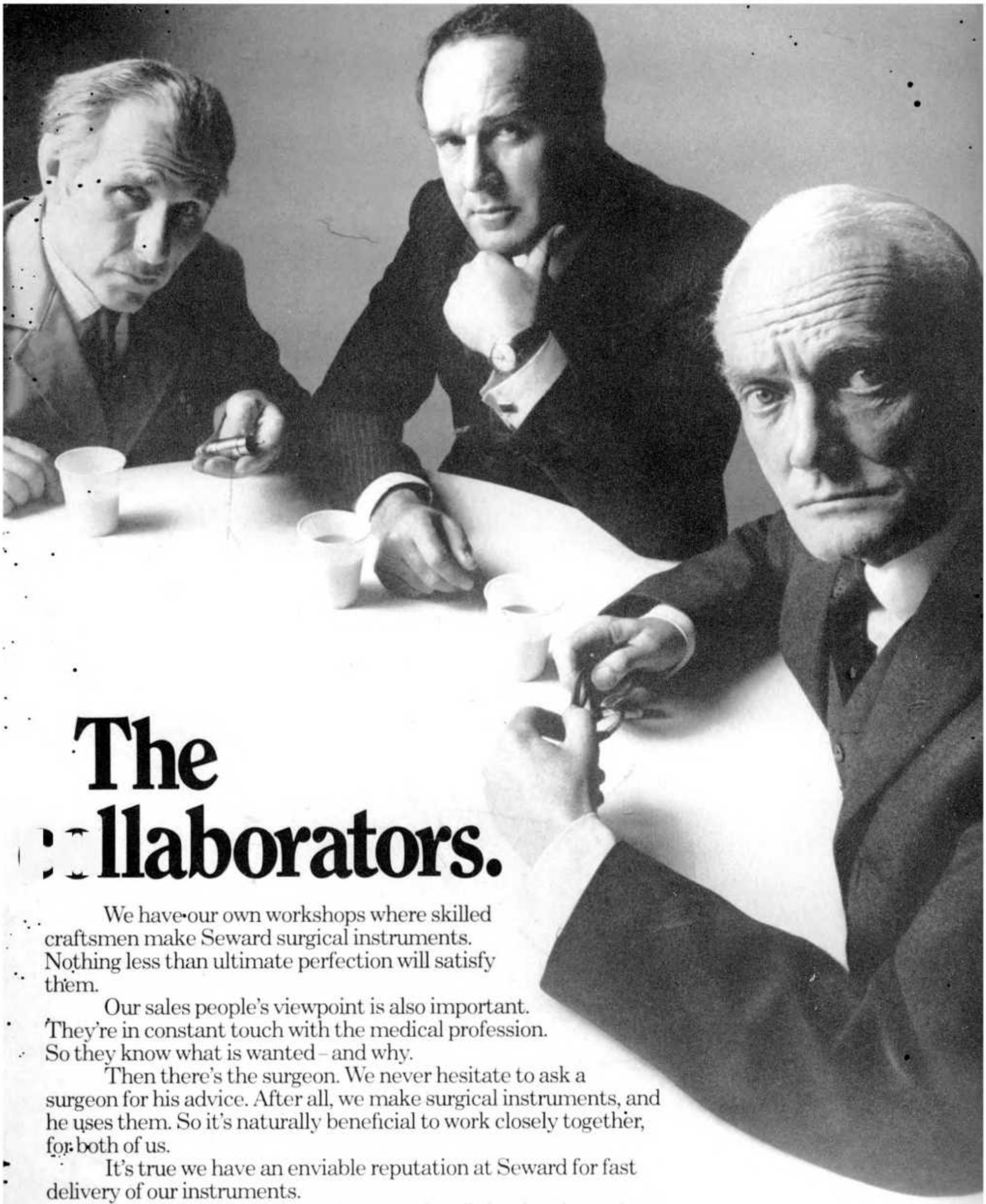
* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX

Subscription £15 per annum, post free. Single copies £1·50, post free

---

THE WILLIAMS & WILKINS CO., BALTIMORE
Second Class Postage paid at Baltimore, and at additional mailing offices.



The Collaborators.

We have our own workshops where skilled craftsmen make Seward surgical instruments. Nothing less than ultimate perfection will satisfy them.

Our sales people's viewpoint is also important. They're in constant touch with the medical profession. So they know what is wanted – and why.

Then there's the surgeon. We never hesitate to ask a surgeon for his advice. After all, we make surgical instruments, and he uses them. So it's naturally beneficial to work closely together, for both of us.

It's true we have an enviable reputation at Seward for fast delivery of our instruments.

But when it comes to design, we take all the time it needs to get things right.

seward – the fast word in quality

A. J. Seward, UAC House, Blackfriars Road, London SE1 9UG.
Telephone: 01-928 7444
A member of the Medical Division of UAC International

The British Journal of Surgery

Vol. 62 : No. 2 : February 1975

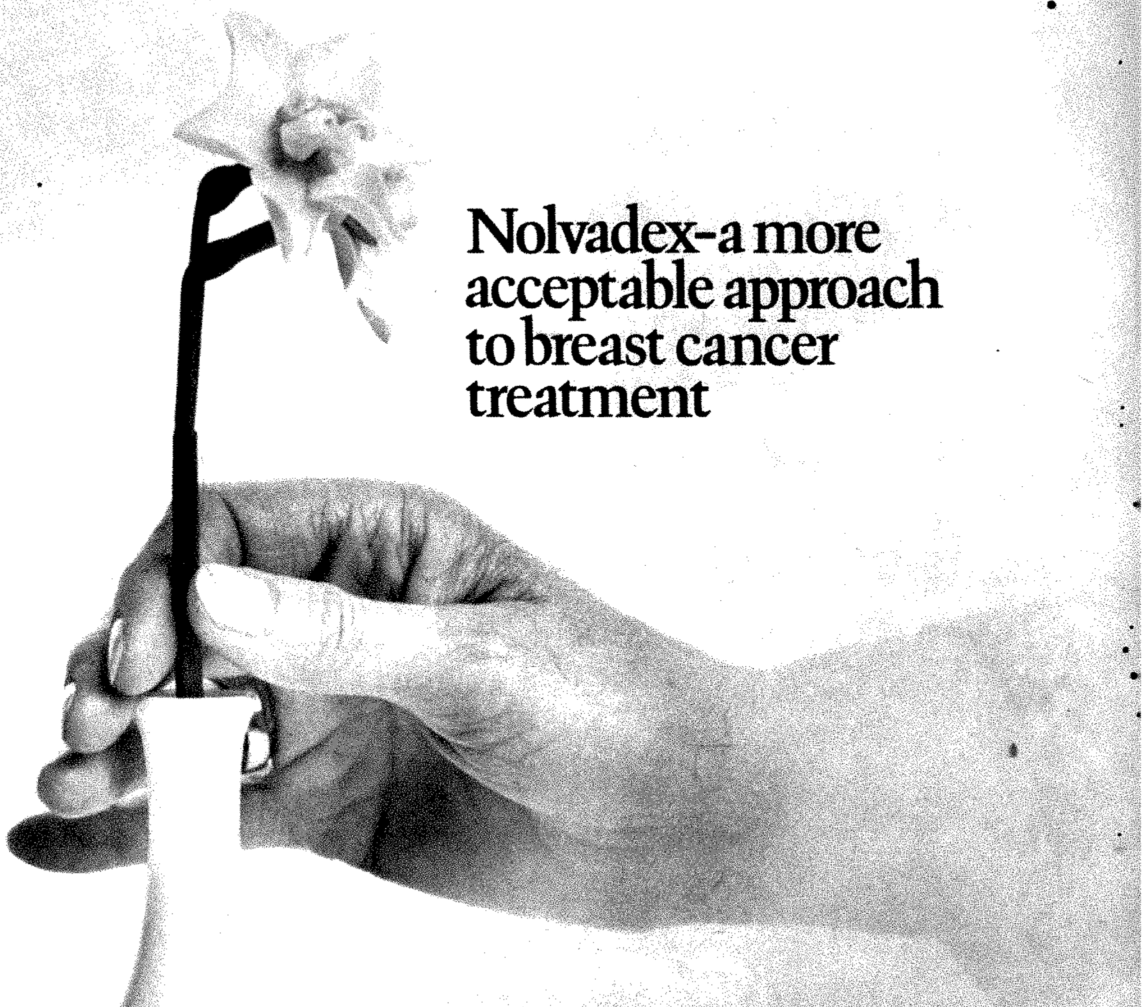
Original papers

		Page
Trans-sphenoidal hypophysectomy in disseminated carcinoma of the breast	P. E. Robin, D. Jean Powell, J. A. H. Waterhouse and G. A. Dalton	85
Raised intracranial pressure due to spinal tumours: 3 rare cases with a probable common mechanism	R. S. Maurice-Williams and J. J. Lucey	92
Arteriographic exposition of the parathyroids	F. Efsen, E. Bruun, K. Lockwood and E. Hasner	96
Nutritional support in the management of external fistulas of the alimentary tract	Victor M. Kaminsky and Mervyn Deitel	100
The treatment of resistant malignant ascites by insertion of a peritoneo-atrial Holter valve	A. V. Pollock	104
Abdominal approach for the ligation of bleeding oesophageal varices	Stanley S. Miller	108
Decreased incidence of indomethacin-induced gastric ulceration in rats by bile duct diversion	Foroogh S. Abtahi and Bijan Djahanguiri	113
The aetiology of hypocalcaemia in acute pancreatitis	John R. Condon, David Ives, Michael J. Knight and John Day	115
An appraisal of peritoneal lavage in the diagnosis of the acute abdomen	Christine Evans, A. Rashid, I. L. Rosenberg and A. V. Pollock	119
Abdominal lavage in blunt trauma	William Gill, Howard R. Champion, William B. Long, Joseph Jamaris and R. Adams Cowley	121
Extrinsic duodenal obstruction in infants and children	G. Tryfonas and D. G. Young	125
Carcinoma of the pancreas and periampullary region: a clinical study in a district general hospital	D. J. T. Webster	130
A comparison of one layer and two layer techniques for colorectal anastomosis	W. G. Everett	135
Complete disappearance of popliteal arterial thromboses in 2 patients	Kenneth Bloor and Victor Cope	141
Long term review of the results of rubber band ligation of haemorrhoids	David M. Steinberg, H. Liegois and J. Alexander-Williams	144
Cervical spinal interbody fusion with Kiel bone	P. S. Ramani, R. M. Kalbag and R. P. Sengupta	147

Surgical Research Society 151

Reviews and notices of books 165

© John Wright & Sons Ltd and the respective contributors named above, 1975.
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.



Nolvadex-a more acceptable approach to breast cancer treatment

Drug therapy is often both uncomfortable and distressing for the patient with advanced breast cancer. But now a more acceptable treatment is available for such patients, 'Nolvadex' (tamoxifen).

'Nolvadex' is an oestrogen antagonist. Whilst it is just as effective as other treatments, it has no hormonal properties. Virilization – common with androgens – is unknown; oedema, nausea and vomiting occur much less frequently than with oestrogens.

'Nolvadex' is taken as twice-daily oral doses. So treatment is simple as well as more acceptable.

Further information – including the results of U.K. trials with 'Nolvadex'[1,2] is available on request.
References: 1 *British Journal of Cancer* (1971), **25**, 270.
2 *British Medical Journal* (1973), **1**, 13.

ICI Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

THE QUEEN'S AWARD TO INDUSTRY [illegible]

Nolvadex
Easier to give, easier to take

'Nolvadex' is a trade mark

PHX

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 60. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are two or more authors (apart from the main author), these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title

of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature* (*Lond.*) **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea 4, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th ed. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology.* London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BEAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

Congress Proceedings

CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding. or that following.,

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)

New and Revised 11th Edition

A SYNOPSIS OF SURGICAL ANATOMY

Edited by D. J. du PLESSIS,
CHM (RAND), FRCS (ENG)

Head of the Department of Surgery,
University of Witwatersrand, Johannesburg;
Chief Surgeon, Johannesburg General Hospital

A general revision has been undertaken to bring the whole book up-to-date and also to eliminate those sections which were not absolutely essential because it is important to prevent a book of this type from becoming too large.

In preparation

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

SENIOR SURGICAL SPECIALISTS

Salary £5,316 + Tax Free Gratuity

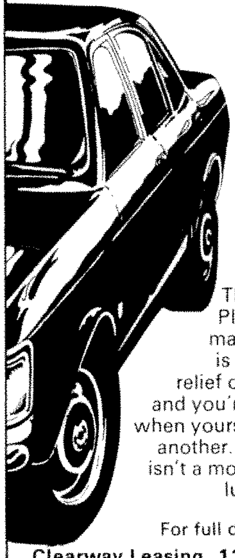
Senior Surgical specialists are required for central hospitals in Malawi. They will work as general surgeons and from time to time give specialist opinions to the Ministry of Health.

Candidates aged 25–55 should hold a qualification registerable in Malawi and post-graduate training in general surgery equivalent to fellowship of the Royal College of Surgeons.

Generous paid leave with free passages and baggage allowance. Education allowances and subsidised housing. Loan for the purchase of a car. Free medical attention.

Please apply to MALAWI BUYING AND TRADE AGENTS, Recruitment Section, c/o Berners Hotel, Berners Street, London W1A 3BE for application form and further details quoting reference number 806/B.

Malawi



NEW CAR?

NO CAPITAL OUTLAY

The Clearway Executive Leasing Plan offers you the choice of any make or model, what's more there is no capital outlay and 100% tax relief on your annual leasing charges, and you're never without a car, because when yours is being serviced we lend you another. For the professional man there isn't a more economical way of ensuring luxurious, trouble free motoring.

For full details contact:
Clearway Leasing, 11 Belmont, Lansdown Road,
Bath BA1 5DZ (Tel: 60463)
An Oliver Rix Company

BURNS Including Thermal Injury

The Journal of the International Society for Burn Injuries

Editor J. E. LAING, FRCS

Published Quarterly: September, December, March, June.

Annual Subscription £8·50 (post free)
Single Numbers £2·40 (post free)

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

CHARLES C THOMAS • PUBLISHER

BLOOD COMPATIBLE SYNTHETIC POLYMERS: An Introduction *by* **Stephen D. Bruck,** *National Institutes of Health, Bethesda, Maryland.* Intended for investigators and students in biomedical curricula and polymer science. Organized in three chapters, the book first gives an outline of macromolecular science with biomedical application in mind. The second chapter discusses the biological environment with specific references to hematological and physiological considerations, neither of which may be familiar to many physical scientists. The third chapter stresses the important problem areas in the interaction of blood with synthetic materials. *'74, 144 pp., 69 il., 14 tables, $9.75*

SAFE CENTRAL VENOUS NUTRITION: Guidelines for Prevention and Management of Complications *by* **Mohamad H. Parsa, Jose M. Ferrer** *and* **David V. Habif,** *all of Columbia Univ., New York.* A comprehensive text prepared for the clinician and investigator engaged in intravenous feeding. A practical guide emphasizing technical and metabolic knowledge required to prevent the potential complications of this treatment. Complications that may occur during placement of central venous catheters and their long-term maintenance are discussed. Also considers methods of infusion, laboratory tests necessary for proper dosage, and metabolic complications such as hypoglycemic reaction. *'74, 280 pp., 132 il., 43 tables, $17.50*

REHABILITATION OF THE FACIALLY DISFIGURED: Prevention of Irreversible Psychic Trauma by Early Reconstruction *by* **J. J. Longacre,** *Univ. of Cincinnati, Cincinnati, Ohio. (2 Contributors)* Observations of the psycho-socio-economic effects of wounding over a period of more than thirty years are presented. This work points out the difference in the effect of early versus late definitive care and its long-range results, especially of the congenitally deformed before they have been exposed to repeated traumatic experiences when they leave the shelter of their homes. Stressed is the importance of the immediate definitive care of severe facial wounds with associate multiple fractures during the first six to eight hours following injury which produces gratifying restoration of individuals who otherwise would become permanently mutilated. *'73, 144 pp. (7 x 10), 384 il., 2 tables, $14.75*

BILIARY TRACT SURGERY AND CHOLANGIOGRAPHY *by* **Vernon L. Stevenson,** *Univ. of Utah Hospital, Salt Lake City.* This book was written to emphasize the importance of operative cholangiography to the surgeon unfamiliar with this technique. Operative cholangiography has led the way to other diagnostic techniques such as angiography and other methods of localizing abnormalities. The second most common operation, that of the biliary system, is extremely technical. Operative injuries to the biliary tract that can be avoided are discussed, and certain cardinal rules for the avoidance of these disasters are provided. *'73, 200 pp., 41 il., $11.50*

THE PORTAL VENOUS SYSTEM *by* **Charles Marks,** *Louisiana State Univ. School of Medicine, New Orleans. Introduction by* **Isidore Cohn, Jr.** Although a great deal of literature exists on various aspects of liver disease, portal hypertension and the anatomy of the portal venous system, this volume places in comprehensive perspective the interrelated information regarding the portal venous system. It effectively utilizes a combination of embryologic and anatomic data in relation to clinical aberrations of the normal and their relationship to clinical problems. *'73, 160 pp., 57 il., $12.75*

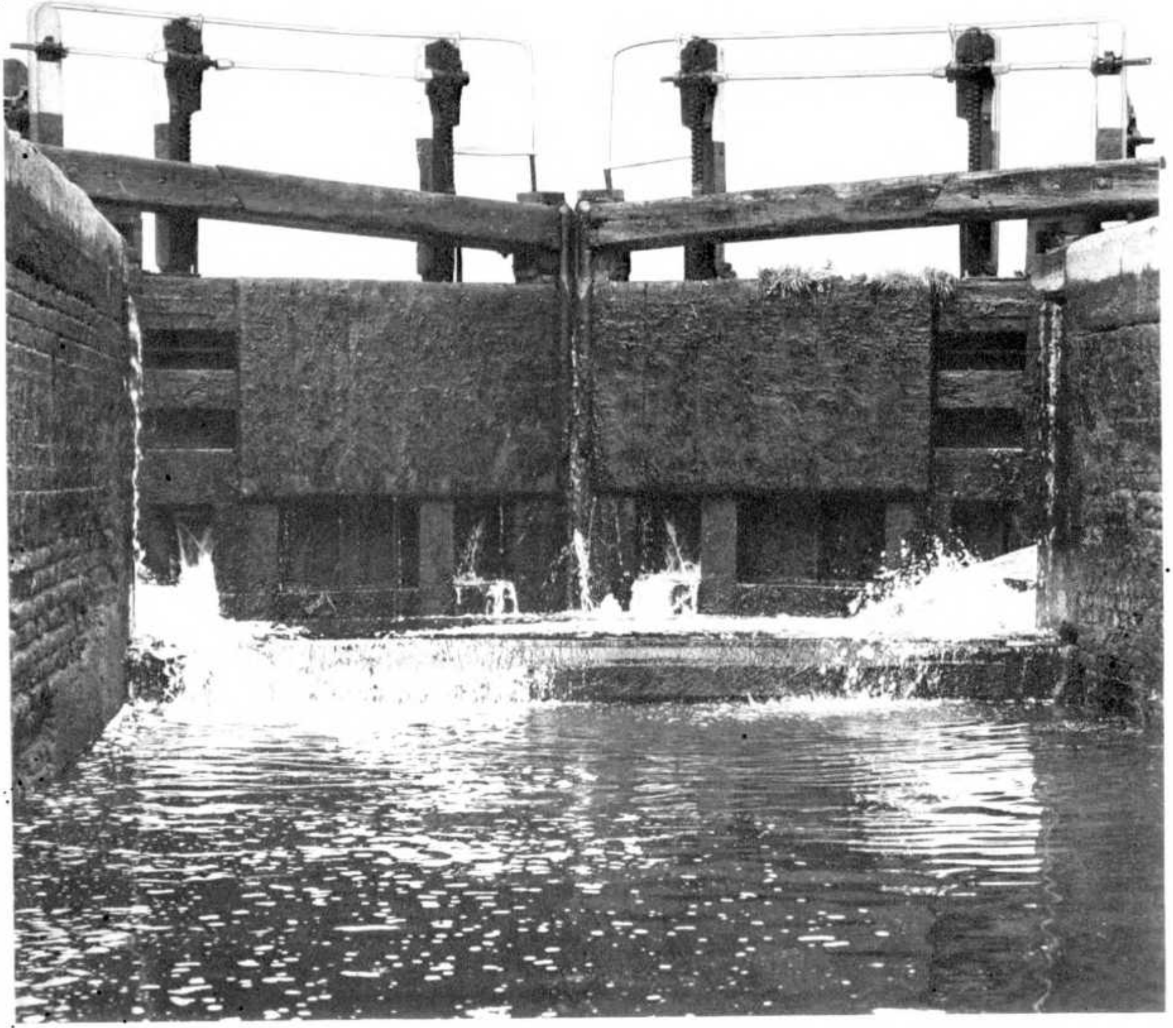
CARCINOIDS OF THE GASTROINTESTINAL TRACT *by* **Richard J. Sanders,** *Univ. of Colorado, Denver.* This book covers the history, histochemistry, biochemistry, pharmacology, physiology, clinical features and treatment of carcinoid tumors. The surgical management and prognosis of carcinoid tumors in each area of the gastrointestinal tract is discussed. All of the currently used forms of treatment are covered. *'73, 148 pp., 23 il., 14 tables, $13.75*

ACUPUNCTURE FOR PHYSICIANS *by* **Teruo Matsumoto,** *Hahnemann Medical College and Hospital, Philadelphia.* All acupuncture points are described in Japanese and Chinese. In addition, these names have been converted to familiar medical nomenclature for physicians. Liberal use of photographs, figures and tables facilitate in the understanding of this art. Special efforts were made to provide information in a very concise manner integrating acupuncture into modern medicine practiced throughout the world as another ancillary tool for the care of patients. *'74, 224 pp. (6 3/4 x 9 3/4), 175 il. (3 in full color), 6 tables, $14.75*

Orders with remittance sent by air, postpaid

301-327 East Lawrence Avenue • Springfield • Illinois • 62717 • USA

A new concept in the control of occlusive vascular disease

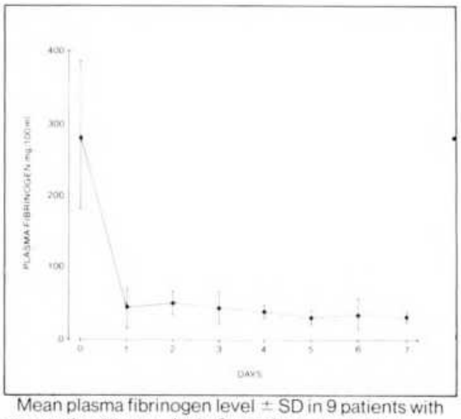


x

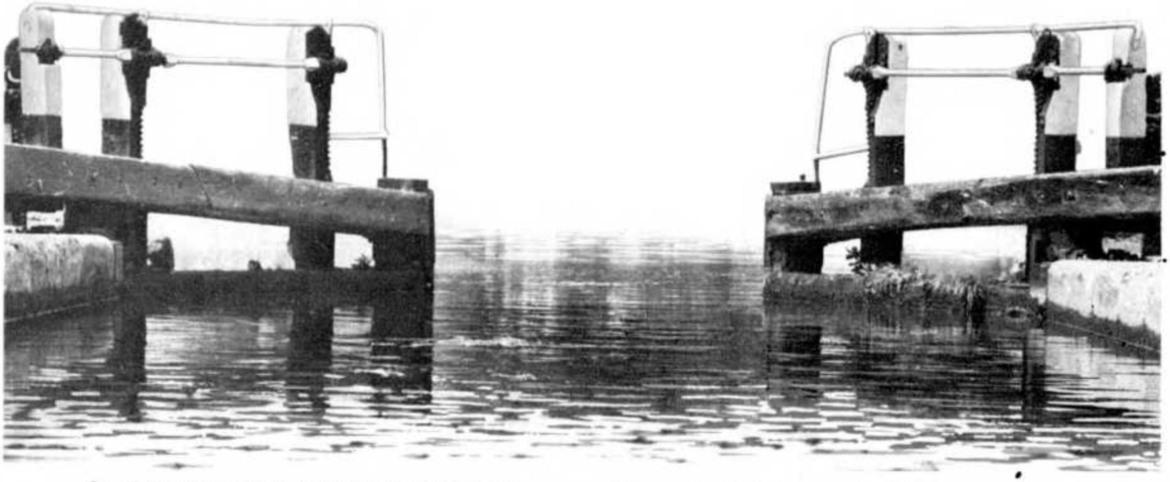
A unique drug is now available to the specialist for routine anticoagulant therapy, and to the researcher as an aid to the elucidation of thromboembolic disorders. Its name is Arvin.

Arvin reduces plasma fibrinogen to a level that maintains marked hypocoagulability without serious spontaneous bleeding complications. This desirable effect is achieved through the specificity of Arvin for fibrinogen—other clotting factors are unaffected.

This state of 'pure' defibrination has an important clinical place when prophylactic measures need to be taken in occlusive vascular disease. e.g. to prevent the formation and extension of thrombi and the dissemination of emboli.



Mean plasma fibrinogen level ± SD in 9 patients with venous thromboses. Arvin 2 units/kg body weight intravenously every 12 hours. From Pitney WR. (1971). Thromb. Diath Haemorrh, *45*, 43.



Consistent features of Arvin therapy include an absence of thromboembolic events during treatment, absence of fibrinogen rebound and low incidence of rethrombosis after treatment has ceased. On withdrawal, plasma fibrinogen returns to haemostatic levels within 12 hours and to normal after 10-20 days. Thus, the changeover to oral anticoagulants is smooth and complication-free.

A consistent dose-effect relationship which ensures simple and precise control methods has been established for Arvin. On this basis, we can recommend this drug for a range of indications where controlled therapeutic defibrination is desirable.

For instance, deep vein thromboses, central retinal and branch vein thrombosis, priapism, pulmonary hypertension of embolic origin, embolism after prosthetic cardiac surgery and rethrombosis after thrombolytic therapy have been shown in clinical trials to respond well to Arvin.

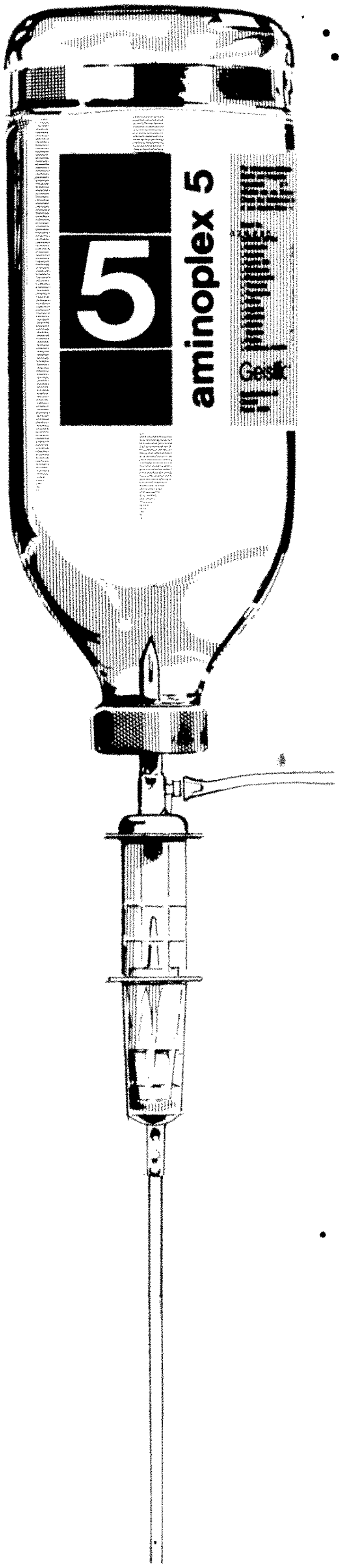
To find out more about the unique Arvin concept specialists are invited to write to us for detailed clinical literature and prescribing information.

Arvin
ancrod
controlled therapeutic defibrination

Berk Pharmaceuticals. Shalford, Surrey.

Arvin is a registered trademark

The single solution
for parenteral nutrition



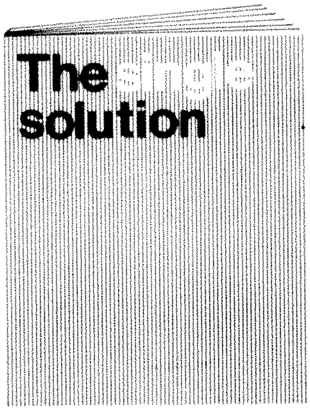
Aminoplex 5

1 litre three times per day provides 15g. of utilisable nitrogen and 3000K calories; the nutrient content being derived from synthetic L-Form amino acids, sorbitol and alcohol.

Geistlich
Chester

In co-operation with Salvia-Werk G.m.b.H., Homburg/Saar, W.Germany.

Medical literature
available from:
Geistlich Sons Ltd.,
Newton Bank,
Long Lane,
Chester CH2 3QZ.
Telephone
Chester 47534-7



The British Journal of Surgery

Vol. 62 : No. 2 : February 1975

Br. J. Surg. Vol. 62 (1975) 85–91

Trans-sphenoidal hypophysectomy in disseminated carcinoma of the breast

P. E. ROBIN, D. JEAN POWELL, J. A. H. WATERHOUSE AND G. A. DALTON*

SUMMARY

One hundred and eight patients with advanced carcinoma of the breast were treated by trans-sphenoidal hypophysectomy and followed up for at least 1 year. The results were assessed both by clinical response and objectively by survival following hypophysectomy, as expressed by the survival ratio. The two methods showed close correlation.

The results show that there is a variation in response relating to menopausal status and age at diagnosis, subsequent hormonal manipulation and physical condition at hypophysectomy. Younger patients whose carcinoma is diagnosed after menopause carry a good prognosis, yet the older premenopausal patients, especially if their clinical condition is poor, do not benefit. Easily available clinical information can be a guide to prognosis.

OF a series of trans-sphenoidal hypophysectomies, 108 consecutive patients who have been followed up for at least 1 year have been analysed. These patients were referred by surgeons, radiotherapists and physicians from the area covered by the Birmingham Regional Cancer Registry. Their ages at hypophysectomy ranged from 33 to 73 years, but at the time of diagnosis they were between 30 and 69 years. All the patients had had some previous treatment before being referred for hypophysectomy. When referred there was clinical evidence of extension of disease beyond the regional nodes.

Of 112 patients who were referred, 2 were rejected because of chronic sinus sepsis and 2 because the pituitary fossa was grossly destroyed by tumour. There was no other selection, and no preoperative test was used to predict response. Thus all patients were accepted for palliative operation whatever their clinical condition. Details of the operation have been described previously (Kapur and Dalton, 1969).

The assessment of the effect of various treatments of carcinoma of the breast has always been difficult. There is controversy even about the results of mastectomy (Crile, 1968), the earliest and most obvious procedure. To assess the effect of hormonal manipulation is in many ways more difficult since by the time such a procedure is adopted a multiplicity of treatments may have already been applied; yet in some ways it is easier since each subject is nearer the termination of life, and it is possible to use death or its delay—that is survival—as a measure of response.

A further complication in assessment is provided by the biological variation in tumour behaviour in carcinoma of the breast. Few tumours are associated with such variation and unpredictability. Assessment of response to a therapeutic procedure must take this into account. Our method proposes a means by which this may be done.

Calculation of survival ratio

Hypophysectomy is generally recommended for cases of carcinoma of the breast where there is evidence of spread beyond the regional nodes. Another way to describe this state would be to say that had the condition been such at the initial diagnosis the case would have been called stage IV (Paterson et al., 1950). We have described the time of initial diagnosis as *P* (*Fig.* 1), and the appearance of the recurrence or metastasis as *M* (i.e. the relevant extension). It is well known that some cases present initially with clinical metastatic disease, while others do not do so for many years—20 or more on occasions. One would anticipate that the case presenting with an early metastasis (*P–M* is short) will have a relatively more aggressive cancer and a worse prognosis, while one without metastasis for many years (*P–M* is long) will be the reverse. This assumption, which is fundamental to our concept, is demonstrated in the figures of the Birmingham and any Cancer Registry.

The actual survival time of patients who had undergone hypophysectomy was assessed and related to the expected survival, taking into account the rapidity

---

* Department of Otolaryngology, Queen Elizabeth Medical Centre, Birmingham, and Birmingham Regional Cancer Registry.

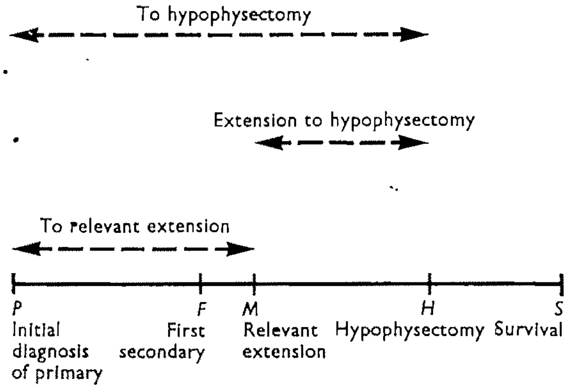


Fig. 1. Diagrammatic representation of the intervals used to calculate the survival ratio. Survival is calculated to the endpoint of survey or death. Any of the following points may coincide (with the consequence that the interval between is zero): *P* and *F*; *F* and *M*; *P, F* and *M*; *M* and *H*; *H* and *S*.

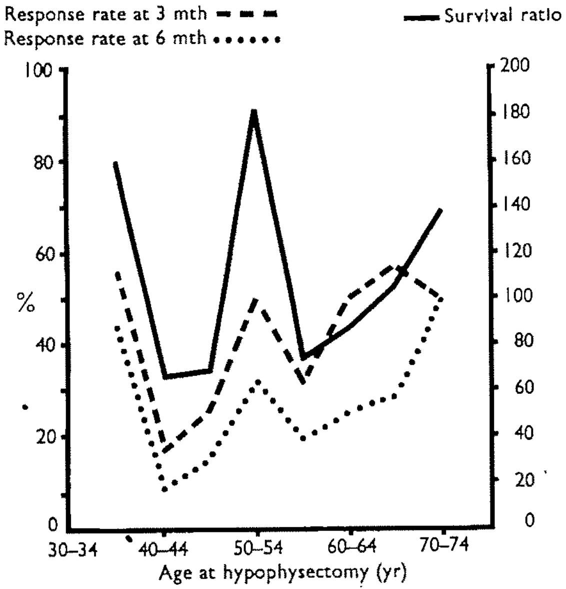


Fig. 2. Survival ratio and response rate compared with age at hypophysectomy.

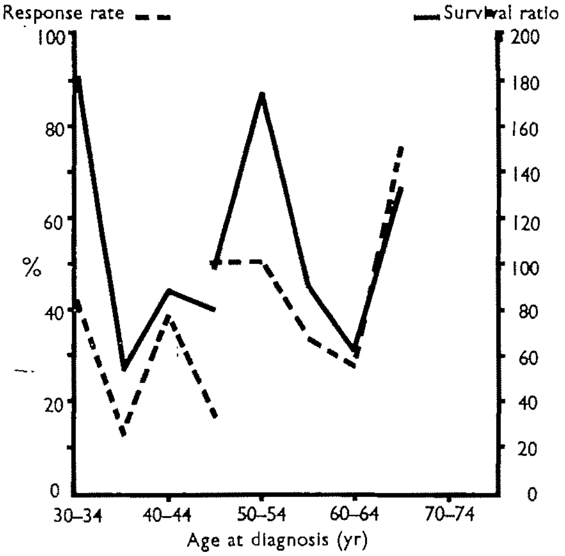


Fig. 3. Survival ratio and response rate compared with age and menopausal status at time of diagnosis.

of the progress of the disease. For example, an individual with a short *P–M* interval would, on average, have a short life expectancy. If hypophysectomy were to double the expected survival, we could confidently state that hypophysectomy had produced a response. Conversely should the *P–M* interval be long, life expectancy would be relatively high, and it would be necessary to extend an already relatively long expectancy still further to show a response. As will be seen, other observations of response correlate with this much more objective assessment, the *survival ratio.*

Controls

From the records of the Birmingham Regional Cancer Registry all the cases diagnosed as suffering from carcinoma of the breast during 1960–4 were collected. (The Registry covers the same area as that from which our hypophysectomy cases are referred.) Altogether 8329 cases were recorded. Because the hypophysectomy cases were within the age range 30–69 years, only those in this age range were used as controls. The number was thus reduced to 6202. Of these, only 2199 were recorded as having developed a relevant extension (*M*), the criterion which could make such a patient a candidate for hypophysectomy. Thus a control group of 2199 cases was obtained. The detailed life expectancies of the 1960–4 control patients were compared with those of a previously well-studied series of patients diagnosed during 1936–50; it was found that the prognosis of the disease had not substantially changed over this long period. The 2199 control cases were then grouped by age and by stage (*Tables I, II*) at initial diagnosis. The control series will be seen to match the larger regional group closely by age. (That the hypophysectomy group does not do so is probably due to the tendency for hypophysectomy referrals to include a higher proportion of younger candidates, a reflection of the preference of the referring practitioner.) However, the control series does differ markedly from both the regional and hypophysectomy groups in its stage distribution. The shift towards the later stages is a reflection of the fact that the controls were chosen to be patients who had either at the time of diagnosis or later developed a relevant extension (i.e. were of comparable severity to the hypophysectomy group). Thus all patients who presented as stage IV are included among the controls. The higher proportion of stage I cases in the hypophysectomy group is likely to be a reflection of their better physical condition which would influence their referral. Discrepancies, whether in age or stage, do not, however, invalidate the assessment since comparisons were made by selecting for each hypophysectomy case the appropriate stage and age groups from the control series.

This was done by forming subdivisions according to stage within each age group; thus for the age group 30–4, subgroups were made according to clinical (and pathological) stages, and likewise for all other age groups. For each subgroup a linear regression equation was developed to summarize in the form of a simple relationship the time between the development of the relevant extension (M) and time before death (S). Since in all cases the fate of our controls was known, our calculations were based on observed facts. Thus, given the age, date of diagnosis (P), clinical stage at diagnosis and the date of the relevant extension (M), we could predict, on the basis of a large number of controls, the expected survival of any individual. By dividing the actual time of survival of a hypophysectomized patient by the expected survival and expressing the answer as a percentage the *survival ratio* is obtained.

Assessment of results

Survival ratio

The effect of hypophysectomy on the survival ratio is demonstrated in *Fig.* 2 where it is related to age at the time of hypophysectomy. It is evident that the proportion obtaining benefit from the operation is variable. Probably the most important feature demonstrable is the parallel relationship between the survival ratio and the response rate. This reassuring finding confirms our previously unsubstantiated belief in the validity of our observations of response rate.

Response rate

This index, adopted by others (Pearson and Ray, 1960), uses an observation of reduction in size or extent of metastases, or subjective improvement in pain or disability. While criticized elsewhere because of lack of objectivity, its close relationship to the objective survival ratio is shown. In addition it is clear from *Fig.* 2 that the response at 3 months is paralleled, at a lower level, at 6 months. No doubt a further reduction would be observed at 12 months. Overall the 3-month rate was 39 per cent but at 6 months was 24 per cent.

Factors affecting prognosis

Both response rate and survival ratio show relationships with menopausal status and age at diagnosis, and with preoperative physical condition.

Age and menopausal status

That the menopause is a significant feature is shown in *Fig.* 3, the pre- and postmenopausal response rates at 3 months being 28 and 44 per cent respectively. Age is that at diagnosis, as is the menopausal status. (All the premenopausal cases in our series had had a natural or artificial menopause before referral for hypophysectomy.) Hypophysectomy is less favourable in patients whose carcinoma is diagnosed before menopause, and becomes even less favourable as the nearness to menopause increases. Conversely the best response rate (50 per cent) is in those who are postmenopausal but relatively younger at the time of diagnosis (*Table III*). This is likewise reflected in the survival ratio (*Table IV*).

Table I: DISTRIBUTION BY AGE AT INITIAL DIAGNOSIS (TRUNCATED AGE RANGE)

Age (yr)	Regional series (%)	Hypophysectomy series (%)	Control* series (%)
30–34	2·5	11·1	2·4
35–39	6·0	8·3	5·5
40–44	11·7	16·7	10·1
45–49	16·0	21·3	14·2
50–54	16·2	17·6	18·1
55–59	16·9	11·1	18·2
60–64	15·8	10·2	16·8
65–69	14·9	3·7	14·7
Total no. of cases	6202	108	2199
Mean age	53·8	48·4	54·3

Table II: DISTRIBUTION BY STAGE AT INITIAL DIAGNOSIS

Stage	Regional series (%)	Hypophysectomy series (%)	Control series (%)
I	44·4	41·5	26·6
II	24·5	25·5	22·4
III	17·2	18·9	23·4
IV	13·9	14·1	27·6
Total staged	4389	106	2199

Includes only cases aged 30–69 years at time of initial diagnosis but excludes those without clinical staging.

Physical condition preoperatively

This factor was graded into three levels: 'fit', 'moderate' and 'poor' (*Table V*) according to the criteria listed. *Table VI* shows the mean survival ratio for each group. In each category the poor group fared badly. Because 3 patients exceeded their life expectation by more than ten times, these were excluded owing to the possibility that their inclusion might distort the results; however, the results are not materially affected. It is of course significant that postoperative deaths occurred only in the moderate and poor groups and amount to 10 per cent, though only 2 per cent can be attributed to surgery.

Physical condition and menopausal status

The combination of these two factors provides the best index of prognosis that we have found. Patients who were premenopausal at diagnosis and whose physical condition was poor fared uniformly badly (0 per cent response) with hypophysectomy (*Table VII*), while the converse was true for the postmenopausal and fit (83 per cent).

Previous hormonal treatment

In 70 per cent of the subjects previous hormonal treatment, either administration of hormones or glandular ablation, had taken place so that some assessment of each subject's response to hormonal

Table III: RESPONSE RATE AT 3 MONTHS COMPARED WITH AGE AND MENOPAUSAL STATUS AT TIME OF INITIAL DIAGNOSIS

	All cases		Premenopausal		Postmenopausal		At menopause or NK	
Age (yr)	No.	%	No.	%	No.	%	No.	%
30–34	12	41·7	12	41·7	—	—	—	—
35–39	8	*12·5*	8	*12·5*	—	—	—	—
40–44	16	50·0	13	38·5	1	*100·0*	2	*100·0*
45–49	22	31·8	12	16·7	8	*50·0*	2	*50·0*
50–54	18	50·0	1	*0·0*	14	50·0	3	*66·7*
55–59	12	33·3	—	—	12	33·3	—	—
60–64	11	27·3	—	—	11	27·3	—	—
65–69	4	*75·0*	—	—	4	*75·0*	—	—
All ages	103	38·8	46	28·3	50	44·0	7	71·4

In 5 cases the response was not known. Rates based on less than 10 cases are in italic figures.

Table IV: MEAN SURVIVAL RATIO COMPARED WITH AGE AND MENOPAUSAL STATUS AT TIME OF INITIAL DIAGNOSIS

	All cases		Premenopausal		Postmenopausal		At menopause or NK	
Age (yr)	No.	%	No.	%	No.	%	No.	%
30–34	10	181·6	10	181·6	—	—	—	—
35–39	9	52·5	9	52·5	—	—	—	—
40–44	17	111·4	14	88·0	1	163·5	2	248·9
45–49	23	88·1	13	79·1	8	97·2	2	110·7
50–54	18	155·6	1	0·0	15	174·5	2	92·1
55–59	10	90·4	—	—	10	90·4	—	—
60–64	9	62·5	—	—	9	62·5	—	—
65–69	4	133·5	—	—	4	133·5	—	—
All ages	100	110·6	47	97·0	47	118·3	6	150·6

Excludes 3 'outliers' (cases where the survival was more than ten times that expected), and 5 cases (not the same as those omitted from *Table III*) omitted for lack of data.

Table V: ASSESSMENT OF PREOPERATIVE PHYSICAL CONDITION

Poor:	Confined to bed with severe pain Dyspnoea at rest Bilateral pleural effusions Ascites Paraplegia
Moderate:	Impaired mobility with widespread metastases Pleural effusion requiring preoperative aspiration Anaemia requiring preoperative transfusion Renal impairment
Fit:	Relatively minor disabilities Permitted more or less normal daily life

Table VI: SURVIVAL RATIO COMPARED WITH PHYSICAL CONDITION

	Fit		Moderate		Poor	
	No.	%	No.	%	No.	%
All cases	26	223·9	48	198·9	29	47·4
Excluding 'outliers'	25	157·8	46	123·9	29	47·4
Excluding operative deaths	26	223·9	41	232·2	23	59·8
Excluding operative deaths and 'outliers'	25	157·8	39	145·5	23	59·8
Cases omitted for lack of data	2		1		2	

'Outliers': cases where the observed survival was more than ten times that expected.
Omissions are: 2 cases not staged; 2 in which the interval was indeterminate; 1 case who was still alive but for whom the survival ratio <100.

Table VII: RESPONSE RATE COMPARED WITH PHYSICAL CONDITION AND MENOPAUSAL STATUS

	Condition at hypophysectomy					
	Fit		Moderate		Poor	
Status at initial diagnosis	No.	%	No.	%	No.	%
Premenopausal	12	50·0	22	31·8	12	0·0
Postmenopausal	12	83·3	21	38·1	17	23·5

treatment was possible. No clear correlation between previous response and the response to hypophysectomy emerged (*Fig.* 4). Indeed, the survival ratio of 28 patients who had not shown a response was better than that of 46 who had previously responded to hormonal treatment. The types of hormonal treatment which had been received were so various that their evaluation was unreliable, but nevertheless two observations can be made. First, previous oophorectomy with adrenalectomy make a good response to hypophysectomy unlikely; secondly, a previous radiation menopause followed by hormonal treatment and then hypophysectomy has not been followed in our experience (13 patients) by any favourable response.

Quality of life after hypophysectomy

When an operation is palliative the subjective attitude is of prime importance. We have made an assessment of the quality of life before and after hypophysectomy. The patients were grouped into three broad categories:

'normal', able to carry out normal day to day activities or employment; 'restricted', where employment, shopping, etc., was limited; 'poor', where the patient was more or less housebound, unable to walk without an attendant or manage her own home or was bedridden. The assessment was made without reference to response.

Table VIII compares these groups. In general, improvement in the quality of life and our assessment of response went hand in hand. Whether the deterioration associated with non-response was a result of operation is unclear.

Discussion

Though others have demonstrated that hormonal manipulation in general and hypophysectomy in particular can produce a good response in patients suffering from carcinoma of the breast (Pearson and Ray, 1960) there have been difficulties in assessment.

These difficulties have been overcome by the use of a survival ratio, because it is both objective (since it relies on an objective measurement—death) and calculated on a follow-up period which is indefinite and independent of a specific time. The close comparability between results using the survival ratio and response rates should also counter suspicion of the latter.

The age of the subject has been quoted as relevant (Harrold et al., 1968), it being generally accepted that younger sufferers are most likely to have hormone-dependent tumours. We do not differ from this view, but would stress that the relationship is not direct, and is complicated by the menopause. That the menopause is involved is evident from the results of assessing together age and menopausal status at the time of diagnosis; so much so that we can only emphasize the observation of Harrold et al. (1968) that subjects who are approaching menopause (especially those with a late menopause) are relatively poor candidates for hypophysectomy. Our findings agree generally with others (Boeson et al., 1961; Edelstyn et al., 1968).

Other writers have used the results of previous hormonal treatment to predict a good or bad response to hypophysectomy (Boeson et al., 1961; Edelstyn et al., 1968). Our own series does not support them, for there are inconsistencies. If we were to draw any conclusion, it would be that previous hormonal manipulation had already 'used up' the response, but because of the variation and variety of therapies, we feel that no firm conclusion is justifiable.

The use of tests predicting response has not been practised by us. Of the many predictive factors and tests (Fairgrieve, 1965), we are impressed by only two. The measurement of urinary 17-hydroxycorticosteroids and aetiocholanolone (Bulbrook et al., 1960) is reasonable but lacks real accuracy, while the stimulation of hypercalcaemia using stilboestrol, attributable to Emerson and Jessiman (1956), applies only to patients with skeletal deposits, and may be followed by dangerous hypercalcaemia. The role of prolactin in prognosis has not yet been evaluated (Stoll, 1974).

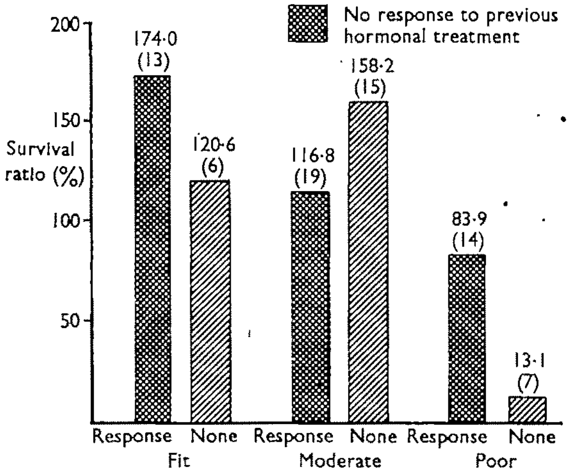


Fig. 4. Survival ratio following hypophysectomy compared with previous response to hormone treatment and physical condition at time of hypophysectomy.

Table VIII: COMPARISON OF RESPONDERS AND NON-RESPONDERS (EXCLUDING OPERATIVE DEATHS)

	Response	No response
Quality of life following hypophysectomy:		
Normal	46·1	4·2
Restricted	51·3	59·6
Poor	2·6	36·2
Compared with before hypophysectomy:		
Improved	89·7	10·6
No difference	7·7	55·3
Deterioration	2·6	34·1
No. of cases assessed	39	47

In 9 patients either the quality of life or response was not known.

The site of secondary deposits has been said to be important; skeletal deposits are said to respond better than most other sites. That this is widely believed is reflected in our finding that a little more than half our cases were referred because of skeletal deposits, while the expected proportion overall would be a quarter (Cole, 1965)—a fact which we can confirm from the Birmingham Cancer Registry figures. We have not sufficient experience of all the possible varieties of sites to make any firm conclusion, but it is our impression that multiple sites are reflected by a very poor physical state, which carries a proportionately bad prognosis.

We agree with Pearson and Ray (1960) that advanced disease leading to a moribund physical state is not likely to be associated with a useful response; also, from our other analyses it is this type of case which suffers the highest mortality in the postoperative period. Since it seems that such cases may suffer a deterioration in the quality of life, we feel that operation should be undertaken with reserve. Nevertheless, since we are content that improvement in life follows any degree of success, we are ready to recommend hypophysectomy as a palliative procedure in patients, especially younger ones, both pre- and post-menopausal, whose physical condition is less than critical, and to view with more reserve those in poor condition, particularly if they were initially diagnosed just before their menopause. Simple easily available clinical data therefore can help to predict many of the poor responders.

Statistical appendix

In this field it is difficult to formulate a method of assessment of the results of treatment which can be generally acceptable. There is an essential subjective element, mainly in terms of the patient's reaction and attitude, but inherent also in the clinician's appraisal, and the comparison of results from different centres is in consequence inevitably complicated by it. We have made use of the *response rate*, which is frequently employed in this field in order to facilitate comparability of results, but we have also developed a quantitative measure, the *survival ratio*, which expresses the actual duration of life with hypophysectomy in relation to that computed from a large control series.

The control group of patients was selected from the totality of cases of breast carcinoma seen in the Birmingham region in the years 1960–4. First, all the patients of the hypophysectomy group were excluded. From the remainder, only patients who had developed a 'relevant extension', in conformity with the definition given in the main text, were chosen, amounting to 2199 patients. The control group was divided into subgroups by clinical stage, pathological grade and 5-year age group. For each subgroup a linear regression equation was calculated between survival (from the time of development of the relevant extension) as the dependent variate, and the interval of time from initial diagnosis to development of the relevant extension as the independent variate.

This method was used because in practice it had proved often difficult, and sometimes not possible, to select an appropriate control case, one for one, on the basis of matching for the three characteristics stated. Two or more potential controls might be equally well suited—or indeed equally badly suited—to an individual hypophysectomy case, leaving an element of choice which was difficult to resolve without the introduction of bias. Moreover, it was not an infrequent finding that the space of time between the development of the relevant extension and the date of hypophysectomy exceeded the duration of life of the control case. To obviate these complications it seemed better to use a statistical method which took account of all the information available from the group of controls of a given age group, stage and grade by summarizing it in the form of a simple relationship (linear regression equation) between the time taken to develop the relevant extension and the subsequent survival.

It was thus possible to obtain for each hypophysectomy case an expected survival based on the behaviour of the appropriate control subgroup, paralleled for stage, grade and age group. However, without further adjustment the two groups would not be fully comparable, because of the interval in the hypophysectomy group from the relevant extension to the time of operation. It would be necessary in order to obtain full comparability to exclude the patients of the control subgroup who had died within this interval, which the hypophysectomy patient had of course survived. The adjustment was made by taking the distribution about the regression line, the mean value of which is the survival calculated from the regression equation, and the standard deviation of which is the 'standard error of estimate', and truncating it. The time to hypophysectomy from relevant extension, measured in units of the standard error of estimate, was used to obtain the point of truncation which would exclude from the calculation the controls whose survival was less than this time interval. The required figure for the expected survival, suitably adjusted for time to hypophysectomy, was then calculated for the section of the distribution remaining after truncation. Having made allowance for the actual survival of the hypophysectomy patient to the time of the operation, the calculated survival was now *an estimate of her further survival after the operation.* By dividing the actual by the expected post-hypophysectomy survival in each case and expressing the result as a percentage, the 'survival ratio' was obtained. When the survival ratio is greater than 100, then that hypophysectomized patient has survived longer than her expectation computed from the control series. The use of the survival ratio combines the advantage of an immediate evaluation of each case in terms of its own computed survival with the knowledge that the maximum of information in the control series has been entered into the computation. The individual ratios can be then treated as numerical assessments of survival when investigating the relevance of any other factors. Calculations of the denominator of the ratio—the expectation—can of course be used to provide an index of prognosis in a case referred for hypophysectomy.

References

BOESON E., SMITH E. J. R. and BARON D. N. (1961) Further experiences with hypophysectomy in advanced breast cancer. *Br. Med. J.* **2**, 790–793.

BULBROOK R. D., GREENWOOD F. C. and HEYWARD J. L. (1960) Selection of breast-cancer patients for adrenalectomy or hypophysectomy by determination of urinary 17-hydroxycorticosteroids and aetiocholanolone. *Lancet* **1**, 1154–1157.

COLE J. O. Y. (1965) Bone metastases in advanced breast cancer: radiological appearances following hypophysectomy. *Clin. Radiol.* **16**, 295–301.

CRILE A. jun. (1968) Results of simple mastectomy without irradiation in the treatment of operative stage 2 carcinoma of breast. *Ann. Surg.* **168**, 330–336.

EDELSTYN G., GLEADHILL C. and LYONS A. (1968) Total hypophysectomy for advanced breast cancer. *Clin. Radiol.* **19**, 426–432.

EMERSON K. and JESSIMAN A. G. (1956) Hormonal influences on the growth and progression of cancer. *New Engl. J. Med.* **254**, 252–258.

FAIRGRIEVE J. (1965) Selective criteria for surgical removal of the endocrine glands in advanced breast cancer. *Surg. Gynecol. Obstet.* **120**, 371–385.

HARROLD B. P., CATES J. E. and JAMES J. A. (1968) Treatment of advanced breast cancer by transsphenoidal hypophysectomy. *Br. J. Cancer* **22**, 19–31.

KAPUR T. R. and DALTON G. A. (1969) Trans-sphenoidal hypophysectomy for metastic carcinoma of the breast. *Br. J. Surg.* **56**, 332–337.

PATERSON R., TOD M. and RUSSELL M. (1950) *The Results of Radium and X-ray Therapy in Malignant Disease.* Edinburgh, Livingstone, pp. 105–106.

PEARSON O. H. and RAY B. S. (1960) Hypophysectomy in the treatment of metastatic mammary cancer. *Am. J. Surg.* **99**, 544–552.

STOLL B. A. (1974) Prolactin in breast cancer. *Proc. R. Soc. Med.* **67**, 291.

> The senior professions of the Church and Law have always had prestige enough to enable each of them to keep a finger firmly and consistently in the governmental pie. They have therefore been able to see to it that any duty that was laid upon them should be set off by a corresponding privilege or immunity. The lowly and junior profession of Medicine, unlike its proud and elder sisters, has had no direct part and no direct influence in the work of government. It has therefore had to submit to its duties being piled up as occasion arose, with no resource for securing a due compensation of privilege and immunity except such slender sense of natural justice as governments possess, and their occasional doubts about the prudence of overloading a willing beast. These resources have shown all the ineffectiveness we might have expected. The result is that at a time when it is no longer possible to conceal the wholly unique importance of medicine for the very existence of social life, that profession finds itself of all professions the least in command of social prestige, the least privileged, the most exposed and the hardest worked.
>
> WILFRED TROTTER, FRS (1933) Address to senior students and junior practitioners. *Med. Wld (Lond.)* **39** (6 October), pp. 123–126.

Br. J. Surg. Vol. 62 (1975) 92–95

Raised intracranial pressure due to spinal tumours: 3 rare cases with a probable common mechanism

R. S. MAURICE-WILLIAMS AND J. J. LUCEY*

SUMMARY

Three cases are reported of raised intracranial pressure associated with spinal tumours. The theories which have been advanced to explain this complication are discussed and it is suggested that in many of the reported cases the underlying mechanism may have been intracranial spread of the tumour and not a blockage of the cerebrospinal fluid pathways with proteinaceous deposits, as has been widely maintained. Autopsy revealed the former process to have operated in 2 of the 3 cases and it may have done so in the third. Two cases had unusual features in common: they were malignant schwannomas (a very rare spinal tumour) and they had both developed within the field of irradiation given for benign conditions many years previously.

RAISED intracranial pressure is a rare complication of spinal tumours situated below the cervicocranial junction, fewer than 30 cases having been reported in the English literature. In most of these cases the exact mechanism has remained uncertain, but it has been widely held that it is related to a raised protein concentration in the cerebrospinal fluid. Three further cases are reported here, and in 2 of them autopsy revealed that metastases had caused hydrocephalus by blocking the cerebrospinal fluid pathways. This may well also have been the explanation in the third case, where an autopsy was not performed.

Case reports

Case 1: A 69-year-old woman was admitted to hospital with pain in the right leg for 18 months, pain in the left leg for 3 months and progressive leg weakness and difficulty in passing urine for 3 weeks. Nineteen years previously she had been given radiotherapy to the lower abdomen after an ovarian cystadenoma had ruptured and seeded into the peritoneal cavity.

On examination she had retention of urine, a flaccid global weakness of both legs and hypalgesia from L5 downwards on the right and S3 downwards on the left. Myelography revealed an irregular intradural block opposite the L3 vertebral body. Cerebrospinal fluid from above the block contained a protein level of 680 mg/100 ml and 17 white cells (15 lymphocytes)/ mm.^{3}

At operation the roots of the cauda equina below the level of L2 appeared thickened and matted together, obliterating the subarachnoid space. The lumbar canal was extremely narrow and a generous laminectomy was performed, leaving the theca open, so that the nerve roots were released from considerable tension. A biopsy of the tissue binding the roots together was reported as showing arachnoidal proliferation but no tumour cells.

Postoperatively there was considerable neurological improvement and it was thought that the patient had a post-irradiation arachnoiditis aggravated by having the chronically inflamed cauda equina confined within a narrow lumbar canal.

Six weeks later her leg weakness worsened again and she became drowsy, confused and complained of headaches. She was readmitted to the neurosurgical unit and found to have bilateral papilloedema, a dense flaccid paraplegia and total sensory loss below the T10 level. Ventriculography revealed a communicating hydrocephalus due to obstruction of the subarachnoid cisterns at tentorial level. The ventricular CSF had a protein concentration of 252 mg/100 ml. It was surmised that the very high CSF protein concentrations had blocked the subarachnoid cisterns.

Insertion of a ventriculo-atrial shunt relieved the symptoms of raised intracranial pressure, but her neurological level gradually rose and she died 6 weeks later when it reached the upper cervical segments. At no time did any cranial nerve or root palsies appear above the main neurological level.

At necropsy the lumbar canal was found to be filled by an irregular tumour of 12 × 5 × 3 cm which was continuous with tumour tissue ensheathing the entire spinal cord and filling the basal cerebral subarachnoid cisterns (*Figs.* 1, 2). A thin layer of tumour thickened the leptomeninges over the brain surface but did not infiltrate the brain parenchyma. The Holter valve system was patent and the ventricles no longer dilated. The other organs of the body were normal and no stigmata of Von Recklinghausen's neurofibromatosis were found.

Microscopy revealed the tumour to be a malignant schwannoma with both compact and loosely textured areas. In the former areas the cells formed parallel rows and interlacing bands with some poorly developed nuclear palisading (*Fig.* 3). Mitotic figures and small areas of necrosis were frequent.

Case 2: A 56-year-old man developed leg weakness and retention of urine following haemorrhoidectomy and was admitted to the neurosurgical unit with a suspected central lumbar disc protrusion. Twenty-seven years previously he had undergone an operation for a lumbar disc protrusion and 21 years before he had been diagnosed as having ankylosing spondylitis and had been given radiotherapy to the thoracolumbar spine to a total dosage of 4800 rad.

On examination he was found to have double incontinence, hypalgesia from L5 down on the right and S3 down on the left, bilateral weakness of dorsi and plantar flexion at the ankle and absent ankle jerks. He had no stigmata of neurofibromatosis. Myelography showed a smooth intradural block opposite the body of L4. The cerebrospinal fluid from above the block contained no cells but had a protein level of 140 mg/100 ml.

At operation the lower roots of the cauda equina were found to be matted together with firm avascular tumour which was partially removed. Microscopy showed a malignant schwannoma composed of elongated spindle-shaped cells in interweaving bundles and large whorls, in areas of variable cellularity (*Fig.* 4). Small necrotic foci marginated by tumour cells were present and mitotic figures were numerous.

Despite a further course of radiotherapy the patient's neurological level began to ascend 2 months later. When it reached the midthoracic level he became confused and lethargic. He was found to have gross bilateral papilloedema, but no root or cranial nerve palsies above the main neurological level. He rapidly became comatose and died. A necropsy was not performed.

Case 3: A 44-year-old man presented in 1968 with remitting pain in the right buttock for 8 years and numbness in the right thigh and progressive weakness of both legs for 18 months. Myelography showed an obstruction at the T12 level and at operation an astrocytoma of the lower thoracic cord was diagnosed. Radiotherapy produced a transient symptomatic improvement, but when this paraparesis worsened a repeat

---

* Departments of Neurological Surgery and Pathology, St Bartholomew's Hospital, London.

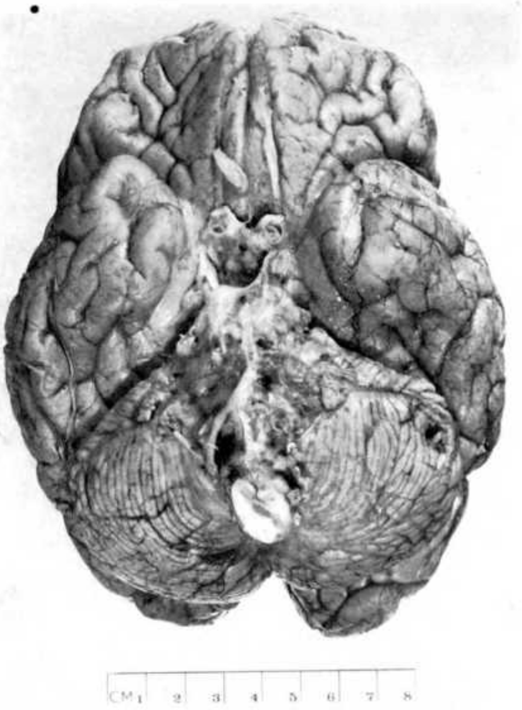


Fig. 1. *Case* 1. Base of the brain showing the basal subarachnoid cisterns filled with tumour.

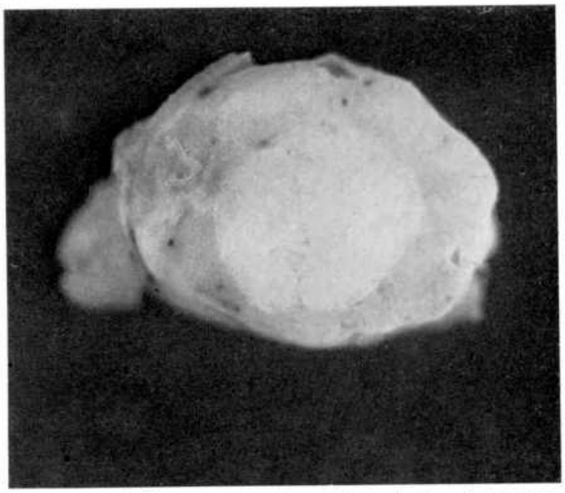


Fig. 2. *Case* 1. Transverse section of the spinal cord showing the coating of tumour.

myelogram in May 1971 showed that the cord swelling had now reached the cervicothoracic junction. Further radiotherapy produced a partial remission and another myelogram in November 1972 showed that the cord expansion had receded to the midthoracic level, at which time his upper level of neurological dysfunction was T3. In mid-1973 he developed personality changes characterized by irritability, drowsiness, apathy and confusion. At the time these were attributed to toxaemia due to trochanteric and sacral pressure sores. He gradually declined and died in September 1973. Other than the mental changes, no neurological abnormalities were apparent at the time of his death above the T1 level.

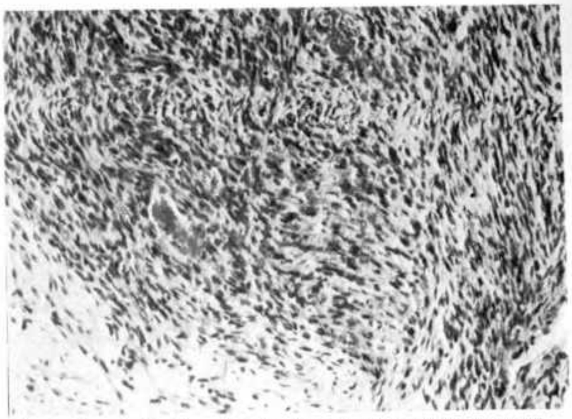


Fig. 3. *Case* 1. Section showing loose and compact areas of malignant schwannoma with poorly formed nuclear palisades (centre). HE. (×90.)

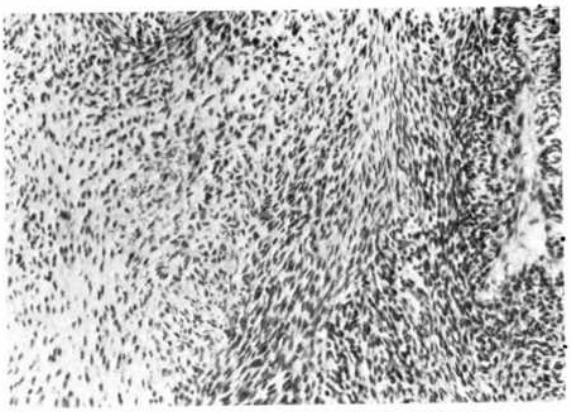


Fig. 4. *Case* 2. Section of the malignant schwannoma showing areas of adjacent compact and loose texture. HE. (×90.)

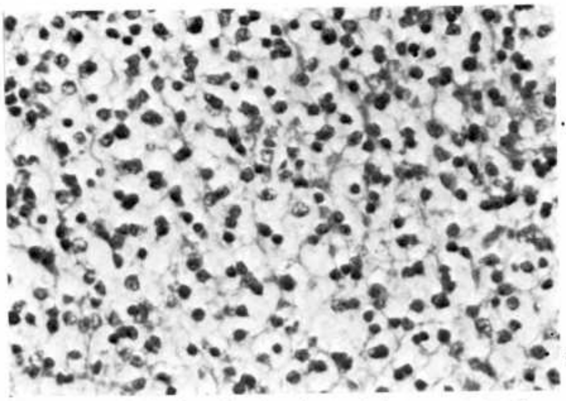


Fig. 5. *Case* 3. Section showing the typical appearance of an oligodendroglioma. HE. (×90.)

Necropsy showed the thoracic cord to be expanded by an intrinsic tumour with a soft haemorrhagic core. The entire fourth ventricle was blocked by tumour, which appeared to have spread up the central canal of the spinal cord in direct continuity with the main tumour mass, otherwise leaving the cervical cord unaffected. The blockage of the fourth ventricle had produced a gross dilatation of the ventricular system.

Histologically the tumour was an oligodendroglioma (*Fig.* 5). The tumour cells were loosely arranged in a delicate fibrovascular stroma. Mitotic figures were infrequent and the nuclei uniform.

Discussion

Spinal tumours situated distantly from the cranial cavity may on rare occasions give rise to raised intracranial pressure and papilloedema. Arseni and Maretsis (1967) reviewed 23 cases from the literature and reported 3 further cases of their own seen amongst 289 spinal tumours over a period of 30 years. Sometimes the symptoms and signs of intracranial hypertension may overshadow or precede those of the primary spinal lesion, so that the latter is overlooked in the search for a cerebral tumour (Neil-Dwyer, 1973).

Various mechanisms have been proposed by which this rise of intracranial pressure might be brought about. As in *Case* 1, metastases carried via the subarachnoid space may block the basal cisterns, causing a communicating hydrocephalus. Such a subarachnoid spread to distant regions by a spinal tumour is believed to be extremely rare. Three cases in which this occurred, a rhabdomyosarcoma and two malignant gliomas, were reported by O'Connell (1946), but in one of these cases the evidence for a subarachnoid spread was tenuous. In *Case* 3 described here, spread up the spinal cord central canal into the fourth ventricle occurred while the main bulk of the tumour was confined to the midthoracic region. A comparable case does not appear to have been reported previously.

In the majority of the cases reported, definite evidence of the underlying pathological process has been lacking and the exact mechanism has been a subject for conjecture. It has been widely held that the same process operates to produce papilloedema in spinal tumours as in the Guillain-Barré syndrome and poliomyelitis (Glasauer, 1964). It is suggested that the high CSF protein blocks the CSF circulation by coming out of solution, either in the basal cisterns (Harris, 1962) or in the arachnoid villi (Denny-Brown, 1952). However, the cause of the raised intracranial pressure in poliomyelitis and the Guillain-Barré syndrome is more likely to be generalized cerebral oedema, as in these conditions air studies have shown that the ventricles are of normal size, and not dilated as in the case of the spinal tumours with papilloedema (Weiman et al., 1951; Joynt, 1958). Joynt (1958) recorded a case of polyneuritis where exploration of one temporal lobe revealed diffuse cerebral swelling with intracellular oedema on microscopy.

In the case of spinal tumours the relationship between the CSF protein level and the presence of raised intracranial pressure is far from clear-cut. The CSF protein is commonly raised above spinal tumours, yet papilloedema is extremely rare. On the other hand, in many of the cases where papilloedema has been reported the protein levels have been raised only moderately, if at all (Love et al., 1951; Mittal et al., 1970). Arseni and Maretsis (1967) found that of 19 cases in the literature where the protein level was recorded, it only exceeded 200 mg/100 ml in 11 and 1000 mg/100 ml in 6. Gibberd et al. (1972) have suggested that a specific protein fraction may be involved, pointing out that in a case which they report the CSF immunoglobulin level was unusually high. These authors also point out that ependymomas —the type of spinal tumour most often reported as producing papilloedema—are particularly liable to subarachnoid bleeding, and that the combination of blood in the CSF and a raised CSF protein may be especially effective in exciting the formation of intracranial meningeal adhesions. Cases have been reported where at operation or necropsy a fibrous arachnoiditis has been found in the posterior fossa (Glasauer, 1964; Arseni and Maretsis, 1967).

In other cases it seems possible that the blockage is at the level of the arachnoid villi. No convincing evidence exists for this having occurred in the case of a spinal tumour, but Denny-Brown (1952) reported a case of polyneuritis where autopsy showed the pacchionian bodies to be blocked with a protein sediment beginning to recanalize. Such a process would fit the fact that in some instances removal of the spinal tumour has been accompanied by regression of the papilloedema (Love et al., 1951). This seems less likely to occur once arachnoid fibrous adhesions have formed, for cases of communicating hydrocephalus due to basal cistern blockage from other causes (meningitis, previous subarachnoid haemorrhage) do not generally resolve spontaneously. Silting up of the arachnoid villi with protein is consistent with the observations of Gardner et al. (1954) that in dogs the addition of autologous serum to the CSF reduces the rate of CSF absorption, although the CSF protein returns rapidly to normal once the protein infusion is discontinued. Recently, however, it has been shown that the CSF–blood junction in the arachnoid villi consists not of a semipermeable membrane against which protein could silt, but of valvular pore connections 7–8 μ in diameter—that is, large enough to permit the passage of red cells, let alone large protein molecules (Welch and Friedman, 1960).

Other postulated mechanisms contributing to the rise of intracranial pressure seem less likely. The suggestion that a complete spinal block will reduce CSF absorption by cutting off absorption via the lumbar sac roots is implausible as so little of the CSF is normally absorbed by this route (Teng et al., 1960). A slowing of CSF absorption by increased CSF osmotic pressure seems ruled out as a protein increase of 300 mg/100 ml will only increase CSF osmotic pressure by 9 mm of water (Gardner et al., 1954). Davson et al. (1970) suggested that CSF flow was reduced owing to the increased protein increasing its viscosity and showed that the rate of absorption was reduced by infusing Dextran, which increases its viscosity.

In few of the reported cases has the responsible mechanism been clearly demonstrated at necropsy. Harris (1962) and Arseni and Maretsis (1967) reported necropsy findings of adhesive intracranial arachnoiditis, and Teng et al. (1960) mentioned that in one case the necropsy revealed metastatic tumour in the basal cisterns. In all case reports a raised CSF protein has been put forward as the major aetiological factor. In this respect the details of *Case* 1 here are instructive. A very high protein level, both above the block and in the ventricles, was found and it was assumed that a protein precipitate was causing the hydrocephalus. The macroscopic appearance of the basal cistern adhesions at necropsy seemed to confirm this, and only microscopic examination revealed the presence of tumour cells. It may well be in fact that in many, perhaps most, of the reported cases such a neoplastic arachnoiditis was present. Two-thirds of the cases reported have been of ependymomas (Arseni and Maretsis, 1967), a type of tumour known to be particularly liable to subarachnoid spread when it occurs intracranially. In some cases biopsies of posterior fossa adhesions have been reported as showing fibrous tissue only (Love et al., 1951), but, as in *Case* 1, a fragment of a neoplastic adhesion may not with certainty allow the identification of tumour cells, and surgically the removal of other than a small piece of a dense adhesion without damaging adjacent structures can be extremely difficult. *Case* 2, where an autopsy was not obtained, might have shown the same mechanism at work as in *Case* 1. However, although metastatic obstruction of the basal cisterns may account for the occurrence of raised intracranial pressure in many of the reported cases, there remains a residue of cases with a benign tumour where this cannot be the explanation, as in 4 of 26 cases reviewed by Arseni and Maretsis (1967), or as in the extradural meningioma with a CSF protein of less than 100 mg/100 ml reported by Mittal et al. (1970).

Cases 1 and 2 have two further and extremely unusual features in common. Both were histologically malignant schwannomas, a type of tumour which has recently been stated to be virtually unknown within the spinal canal (Northfield, 1973), and in both cases the fields of origin of these unusual tumours had been subjected to radiotherapy for an unrelated condition many years before. The relationship of this radiotherapy to the development of these tumours can only be surmised, but earlier reports of central nervous system tumours apparently arising within previously irradiated areas have been extremely few and the tumours concerned have all been of mesodermal rather than of neurectodermal origin (Russell and Rubinstein, 1971).

Acknowledgements

We should like to thank Mr R. C. Connolly and Mr J. C. M. Currie for permission to report cases treated under their care. We are also grateful to Mr P. Crocker for the photomicrography.

References

ARSENI C. and MARETSIS M. (1967) Tumours of the lower spinal cord associated with increased intracranial pressure and papilloedema. *J. Neurosurg.* **27**, 105–110.

DAVSON H., HOLLINGWORTH G. and SEGAL M. B. (1970) The mechanism of drainage of the cerebrospinal fluid. *Brain* **93**, 665–678.

DENNY-BROWN D. E. (1952) The changing pattern of neurologic medicine. *New Engl. J. Med.* **246**, 839–846.

GARDNER W. J., SPITLER D. K. and WHITTEN C. (1954) Increased intracranial pressure caused by increased protein content in the cerebrospinal fluid. *New Engl. J. Med.* **250**, 932–936.

GIBBERD F. B., NGAN H. and SWANN G. F. (1972) Hydrocephalus subarachnoid haemorrhage and ependymomas of the cauda equina. *Clin. Radiol.* **23**, 422–426.

GLASAUER F. E. (1964) Thoracic and lumbar intraspinal tumours associated with raised intracranial pressure. *J. Neurol. Neurosurg. Psychiatry* **27**, 451–458.

HARRIS P. (1962) Chronic progressive communicating hydrocephalus due to protein transudates from brain and spinal tumours. *Dev. Med. Child Neurol.* **4**, 270–278.

JOYNT R. J. (1958) Mechanism of production of papilloedema in the Guillain–Barré syndrome. *Neurol.* (*Minneapolis*) **8**, 8–12.

LOVE J. G., WAGENER H. P. and WOLTMAN H. W. (1951) Tumours of the spinal cord associated with choking of the optic disks. *Arch. Neurol. Psychiatry* **66**, 171–177.

MITTAL M. M., GUPTA N. C. and SHARMA M. L. (1970) Spinal epidural meningioma associated with increased intracranial pressure. *Neurol.* (*Minneapolis*) **20**, 818–820.

NEIL-DWYER G. (1973) Tentorial block of cerebrospinal fluid associated with a lumbar neurofibroma. *J. Neurosurg.* **38**, 767–770.

NORTHFIELD D. W. C. (1973) *The Surgery of the Central Nervous System*. Oxford, Blackwell.

O'CONNELL J. E. A. (1946) The subarachnoid dissemination of spinal tumours. *J. Neurol. Neurosurg. Psychiatry* **9**, 55–62.

RUSSELL D. S. and RUBINSTEIN L. J. (1971) *Pathology of Tumours of the Nervous System*, 3rd ed. London, Arnold.

TENG P., WAGNER J. H. and BUXBAUM M. W. (1960) Giant ependymoma of the spinal cord associated with papilledema. *Arch. Neurol.* **2**, 657–662.

WEIMAN C. G., MCDOWELL F. H. and PLUM F. (1951) Papilledema in poliomyelitis. *Arch. Neurol. Psychiatry* **66**, 722–727.

WELCH K. and FRIEDMAN V. (1960) The cerebrospinal fluid valves. *Brain* **83**, 454–469.

Br. J. Surg. Vol. 62 (1975) 96–99

Arteriographic exposition of the parathyroids

F. EFSEN, E. BRUUN, K. LOCKWOOD AND E. HASNER*

SUMMARY

Arteriographic exposition of the parathyroids in 52 patients consecutively referred for primary hyperparathyroidism is reported. Thirty-nine patients underwent neck exploration. In 29 patients pathologic parathyroids were found. The arteriographic evaluation was based on observation of the course of the inferior thyroid artery and the presence of parenchymal opacification. Comparison of arteriography and surgical findings revealed that selective angiography of the inferior thyroid artery had a high sensitivity and specificity in the detection of pathologic parathyroids far exceeding that of a non-selective technique.

IDENTIFICATION of all the parathyroid glands was established as a principle for surgical exploration over 40 years ago (Churchill and Cope, 1934). The complexity of the clinical findings and the biochemical disturbances present in primary hyperparathyroidism (PHPT) make preoperative visualization desirable. At present angiography appears to be the only method offering a possibility of estimating the volume of even normal parathyroids. Using angiography the course of the inferior thyroid artery can be visualized as proposed by Radner (1949) and described by Seldinger in 1953 and 1954. Parenchymal opacification of parathyroid tissue was described by Doppman et al. (1969). Both criteria have been applied in the present study.

Materials and methods

The present prospective study is based on a consecutive series of 52 patients referred for PHPT; there were 30 men and 22 women with mean ages of 46·1 years (range, 19–76) and 53·6 years (range, 26–78) respectively.

Thirteen of the 52 patients were not operated on because of lack of evidence for the diagnosis. Neck surgery was performed in 39 cases. Decisions to undertake neck exploration were based on anamnestic, clinical, radiological and biochemical data. A diagnosis of PHPT was confirmed at surgery in only 29 of the 39 patients (*Table I*). The ultimate diagnosis of PHPT was based on microscopical examination of the parathyroid glands (Werdelin, 1964).

Retrospectively we have attempted to weight the probability/evidence of correctness of our tentative diagnosis on the basis of the pre-admission history, objective findings, results of conventional radiology and biochemical findings. This classification resulted in the following four groups of different clinical evidence of PHPT: 'evident', 'plausible', 'not to be excluded' and 'unlikely' (*Table I*). The level of serum calcium† showed significant differences between the four groups in spite of wide ranges ($P<0·001$, Mann–Whitney *U*-test). One patient only was classified as 'unlikely'.

Angiography

Bilateral examinations were performed in 46 patients and in 6 patients unilateral examinations were performed, totalling 98 investigations. Twenty-eight angiographs of the inferior thyroid artery were carried out and are referred to as 'selective'. Care was taken that the blood flow around the catheter tip was unimpaired. The remaining 70 angiographs were performed with a lesser degree of selectivity and are referred to as 'non-selective' examinations.

Bilateral and unilateral examinations and selective and non-selective angiographs were equally distributed without significant differences between the 'evident', 'plausible' and 'not to be excluded' groups ($P>0·2$, Fisher's exact probability test).

Torsion stable catheters (Ducor, Cordis Inc., or Torcon, Cook Inc.) were inserted transfemorally during local anaesthesia using the Seldinger method. In all the patients the first catheter inserted was a 'right coronary (5 cm)' which could always be advanced into the left subclavian artery. In cases where this catheter could not be moved from the aorta into the anonymous or right subclavian artery it was replaced by a so-called 'head hunter' catheter. Later in the series the technique was modified into percutaneous catheterization of the right brachial artery using a 'femoral-visceral I' catheter.

The contrast medium used was Urografin meglumine (diatrizoate meglumine, BP) containing 306 mg of iodine/ml. In selective arteriography of the inferior thyroid artery the dose was 5–6 ml injected at a rate of 4–5 ml/sec. The dose in non-selective examinations was 18–20 ml delivered at a rate of 10–12 ml/sec. Radiographs were made in three series, starting at a rate of four per second for 3 seconds, followed by one per second for 4 seconds, and one exposure every third second for the last 12 seconds.

Angiographic evaluation: This was based on findings in the thyroid gland and adjacent structures, especially the mediastinum, as described below:

1. The presence of arteries having a stretched curvolinear course, indicating the probability of a *space-occupying process*.
2. *Parenchymal opacification* within the area circumscribed by the above arteries or placed elsewhere in the neck.

---

* Department of Diagnostic Radiology, Cardiovascular Section and Department of Endocrine Surgery, University Hospital (Rigshospitalet), Copenhagen, Denmark.

† In the present series serum calcium analysis was based on a normal range of 2·30–2·70 mmol/l.

Table I: PROBABILITY OF PRIMARY HYPERPARATHYROIDISM CLASSIFIED ACCORDING TO ANAMNESTIC, CLINICAL, RADIOLOGICAL AND BIOCHEMICAL DATA IN 52 PATIENTS

	'Evident' ($n = 7$)	'Plausible' ($n = 27$)	'Not to be excluded' ($n = 17$)	'Unlikely' ($n = 1$)	Total ($n = 52$)
Serum calcium (mmol/l)					
Median	3·07	2·75	2·47	2·71	
Range	2·93–3·92	2·37–4·13	2·20–3·47		
No. of hypercalcaemic patients	7	18	4	1	30
No. of normocalcaemic patients	0	9	13	0	22
Explored patients	7	24	7	1	39
Hypercalcaemic	7 (7)	17 (16)	1 (1)	1 (0)	26 (24)
Normocalcaemic	0	7 (4)	6 (1)	0	13 (5)

Figures in parentheses indicate number of patients with primary hyperparathyroidism.

The application of these criteria is shown in *Table II*. Except in one case all arteriographic examinations and their evaluation have been carried out by one of us (F. E.) before deciding on therapy.

Non-parametric statistical tests have been used with levels of significance of 0·01 and 0·05 depending on the nature of the hypothesis. However, the probability levels actually associated with our findings are given. *Complications*: The only severe and permanent complication was a right-sided hemiplegia in a man aged 58 years. This occurred during the manipulation of a swan-neck catheter ('head hunter' type) in the aortic arch, and as such was unrelated to our method. One case had a transient spasm in the right brachial artery following removal of the catheter. Additionally, 2 patients experienced an unspecific cerebral reaction of short duration, probably related to the contrast medium.

Results

The criterion 'curvolinear arteries' indicating a space-occupying process is, according to Seldinger (1953, 1954), reliable even when the examination is non-selective (*Table II*). In contrast, parenchymal opacification (Doppman et al., 1969) seems only to be of value in the selective technique (i.e. injection into the inferior thyroid artery). Applying these criteria, the angiographic results for each patient were compared with the surgical findings in the 39 patients in whom neck exploration was performed (*Table III*).

Twenty-nine patients showed PHPT. In the remaining 10 patients PHPT was not found (i.e. no parathyroid adenoma or hyperplasia was identified). Among the 29 patients in whom PHPT was confirmed 3 cases had a normal angiograph and are considered 'false negative'. (In *Table III* the column 'true negative' is shown for the sake of completeness.)

In the 10 patients in whom PHPT was not found during neck exploration, angiography was interpreted as positive for parathyroid adenoma. In 6 cases a lymph node or thyroid adenoma was located at the point indicated by the angiograph. From a purely radiological point of view the anatomical diagnosis was correct and these patients are therefore listed under the heading 'true positive'. In 4 cases the angiographic statement could not be confirmed and the patients are listed as 'false positive'.

Table II: ACCURACY OF ANGIOGRAPHIC PARAMETERS IN PREDICTING THE TOPOGRAPHY OF THE PARATHYROIDS IN 39 PATIENTS UNDERGOING NECK EXPLORATION*

	Selective angiographs ($n = 25$)		Non-selective angiographs ($n = 49$)		
Angiographic finding	Correct	Incorrect	Correct	Incorrect	Total
Curvolinear arteries	6	1	10	5	22
Parenchymal opacification	4	1	2	1	8
Both	5	1	1	3	10
Suspicious	1	1	3	5	10
Normal	4	1	9	10	24
Total	20	5	25	24	74

* Unilateral examination in 4 patients and bilateral in 35 patients.

It is well known that hyperparathyroid patients may be normocalcaemic for relatively long periods of time. The diagnosis nevertheless may be suspected from other biochemical criteria not discussed in the present paper.

In *Tables I* and *III* the patients are divided into normocalcaemic and hypercalcaemic. Thirteen normocalcaemic patients were subjected to neck exploration, 5 of which revealed PHPT. The distribution of the normocalcaemic patients within the clinical subdivision into four groups is shown in *Table I*. In the 'plausible' group PHPT was confirmed in 4 out of 7 normocalcaemic patients, but in the 'not to be excluded' group this diagnosis was only confirmed in 1 out of 6 normocalcaemic patients.

Concerning the clinical application of angiography, all the patients subjected to neck exploration in the 'not to be excluded' group exhibited a positive angiograph. This differs significantly from the angiographic findings in the remaining 10 patients not subjected to neck surgery, as 7 patients showed a normal angiograph ($P < 0{\cdot}01$, Fisher's exact probability test).

A definite evaluation of the angiographic method has been attempted (*Table IV*). Only the 25 patients with histologically verified PHPT having had preoperative bilateral angiography performed were included. From a taxonomical point of view this is

Table III: COMPARISON OF ANGIOGRAPHIC AND SURGICAL FINDINGS IN 39 PATIENTS UNDERGOING NECK EXPLORATION

	PHPT confirmed at operation			PHPT not found at operation		
Angiographic finding	Normocalcaemic patients ($n = 5$)	Hypercalcaemic patients ($n = 24$)	Total ($n = 29$)	Normocalcaemic patients ($n = 8$)	Hypercalcaemic patients ($n = 2$)	Total ($n = 10$)
True positive	3	20	23	4	2	6
True negative*	—	—	—	—	—	—
False positive	—	3	3	4	—	4
False negative	2	1	3	—	—	—

* *See* text.

Table IV: PREOPERATIVE APPLICATION OF BILATERAL ANGIOGRAPHY IN 25 PATIENTS WITH PROVED PRIMARY HYPERPARATHYROIDISM

	Surgery			
	Positive	Negative	Positive	Negative
Angiography	Non-selective angiography ($n = 15$)		Selective angiography ($n = 10$)	
Positive	9	4	10	2
Negative	6	11	0	8
Sensitivity*	60·0		100	
Specificity†	73·3		80·0	

* Sensitivity is defined as the number of correct positive angiographic findings.

† Specificity is defined as the number of correct negative angiographic findings.

justified. Consequently the evaluation of the specificity of the angiographic method has been based on the angiographic and surgical findings in these 25 patients. As 'unrelated structures' do not add to the diagnosis they have been included in the group of 'false positives' even if they were found to be topically correct at surgery.

Analysing the data from *Table IV* in fourfold tables (Documenta Geigy, 1970) the *selective technique* revealed a highly significant correlation ($P < 0{\cdot}01$) between angiography and surgery, in agreement with the specificity and sensitivity recorded. The specificity and sensitivity achieved by the *non-selective* technique were less favourable and no statistically significant correlation could be demonstrated ($P > 0{\cdot}1$). As to the sensitivity of angiography the size of the adenoma in the present distribution of parathyroid adenomas has to be taken into consideration. The median weight of all parathyroids was 549 mg (range 62–5190 mg, $n = 24$). No difference with respect to size of adenoma between the selective and non-selective technique was found ($P > 0{\cdot}1$, Wilcoxon rank test).

Discussion

The surgical conception that a branch from the inferior thyroid artery might be a guide to a parathyroid adenoma instigated the present investigation. The angiographic method can also demonstrate the parathyroids, as seen from the sensitivity and specificity achieved according to the definitions by Burgess et al. (1962). Selective angiography is superior to the non-selective technique (*Table IV*). The reason for this seems to be the predominance of the inferior thyroid artery in the vascular supply of the parathyroid glands (Alveryd, 1968). In accordance with this assumption we regard it as unnecessary to attempt to catheterize the superior thyroid artery. In fact our figures from selective versus non-selective examinations justify this conclusion.

Kuntz and Goldsmith (1972), combining the angiographic method with thyroid scintigraphy in a series of 21 consecutively examined patients with PHPT, reached a sensitivity of about 70 per cent. However, close examination of their figures indicates that the specificity of their method is only 50 per cent or less. Our technique was not supported by other iconographic procedures. On the other hand, the extremely high sensitivity obtained in the present series is probably not fully reproducible. However, we found our material representative of a parathyroid clinic (*Table I*), and the analysis has been based on two angiographs for each patient in order to achieve complete equality and comparability between the observations.

One might argue that the present investigation reflects differences between selective and non-selective techniques caused by irregularities in the arteries concerned. This interpretation, however, neither alters the results nor affects the conclusions of this study.

Because of the angiographic method's independence of biochemical data we found it valuable to include normocalcaemic patients in the study. No significant differences ($P > 0{\cdot}2$, Fisher's exact probability test) concerning correct or incorrect angiography statements were found between the groups of patients with or without PHPT. These findings were explained by the so-called 'unrelated' structures.

Furthermore, only 5 of the 13 normocalcaemic patients revealed pathologic parathyroids. Compared with the results in the 'not to be excluded' group these figures reflect the influence of angiography on our process of decision. Therefore supporting diagnostic procedures to ascertain hyperparathyroidism in normocalcaemic patients are imperative. The only severe complication recorded was related to manipulation of the catheter in the aortic arch. However, even if the risk is very low (Cronquist et al., 1970) it is a risk that is attached to all methods involving passage of a catheter through the aortic arch.

Parathyroid surgery essentially consists of identification of *all* parathyroid tissues. Therefore, application of current radiographic methods appears to be inconsistent, except for cases subjected to re-exploration.

In our experience the angiographic method requires considerable expertise. For this reason we recommend that the method be restricted to parathyroid centres, and principally to patients selected for re-exploration.

In conclusion the results of non-selective arteriographs are insignificant. Selective arteriography of the inferior thyroid artery is a reliable method for visualization of the parathyroids with both a high sensitivity and specificity.

References

ALVERYD A. (1968) Parathyroid glands in thyroid surgery. *Acta Chir. Scand.* (*Suppl.*) **389**, 20.

BURGESS A. M., FEJFAR Z. and KAGAN A. R. (1962) Arterial hypertension and ischaemic heart disease: comparison in epidemiological studies. 2. Definitions and general principles. *WHO Chron* 16. Geneva, WHO, pp. 441–444.

CHURCHILL E. D. and COPE O. (1934) Parathyroid tumors associated with hyperparathyroidism. *Surg. Gynecol. Obstet.* **58**, 255–271.

CRONQUIST S., EFSING H. O. and PALACIOS E. (1970) Embolic complications in cerebral angiography with the catheter technique. *Acta Radiol.* (*Diagn.*) (*Stockh.*) **10**, 97–107.

DOCUMENTA GEIGY (1970) *Scientific Tables*, 7th ed. (ed. DIEM K. and LENTNER C.). Basle, Geigy, pp. 109–123.

DOPPMAN J. L., HAMMOND W. G., MELSON G. L., EVENS R. G. and KETCHAM A. S. (1969) Staining of parathyroid adenomas by selective arteriography. *Radiology* **92**, 527–530.

KUNTZ C. H. and GOLDSMITH R. E. (1972) Selective arteriography of parathyroid adenomas. *Radiology* **102**, 21–28.

RADNER S. (1949) Subclavian angiography by arterial catheterization. *Acta Radiol.* (*Stockh.*) **32**, 359–364.

SELDINGER S. I. (1953) Catheter replacement of the needle in percutaneous arteriography. *Acta Radiol.* (*Stockh.*) **39**, 368–376.

SELDINGER S. I. (1954) Localization of parathyroid adenomata by arteriography. *Acta Radiol.* (*Stockh.*) **42**, 353–366.

WERDELIN O. (1964) The parathyroids in primary hyperparathyroidism. *Acta Pathol. Microbiol. Scand.* **61**, 211–232.

Br. J. Surg. Vol. 62 (1975) 100–103

Nutritional support in the management of external fistulas of the alimentary tract

VICTOR M. KAMINSKY AND MERVYN DEITEL*

SUMMARY

A total of 56 patients with 65 fistulas was treated using one or a combination of three modern nutritional aids. Fifty-two of the fistulas (80 per cent) closed spontaneously and only 7 fistulas (10·8 per cent) required attempts at operative closure. The overall mortality was 7 patients (12·5 per cent), which compared favourably with a 40 per cent mortality in an earlier comparable group which had not received such nutrition.

PRIOR to Dudrick's (1968) classic report, the mortality in patients with fistulas of the alimentary tract ranged from 30 to 50 per cent (Edmunds et al., 1960; Chapman et al., 1964; Halversen et al., 1969). Early resection was recommended for upper small bowel fistulas and expectant treatment for fistulas of the lower bowel as the latter had a higher incidence of spontaneous closure (Edmunds et al., 1960; Bacon and Gennaro, 1969; Lorenzo and Beal, 1969). All agreed that if operation were performed, resection of the involved portion of bowel with anastomosis, if possible, was the treatment of choice.

Chapman et al. (1964) found in their patients with fistulas that those who received more than 3000 kcal/24 hr had a mortality of 12 per cent whereas those who received less than 1000 kcal/24 hr had a mortality of 55 per cent. The former group received the calories by combined intravenous and tube feeding, achieved by passing a tube beyond the fistula or by a feeding jejunostomy.

More recently Voitk et al. (1973), using an elemental diet, had a mortality of 28 per cent, and MacFadyen et al. (1973), treating gastro-intestinal fistulas with intravenous hyperalimentation, had a mortality of 6·4 per cent.

Since 1969 we have used three techniques in patients with major nutritional problems, and in 17 per cent of these patients the indication was alimentary tract fistulas. The results of nutritional support in the management of fistulas have been compared with those in fistulas treated before these methods were available.

Materials and methods

Two groups were reviewed. Group 1 consisted of patients with fistulas treated by modern nutritional methods from July 1969 to December 1973. Group II were patients treated before the introduction of these methods, from July 1965 to July 1969.

Group I

There were 56 patients with 65 external gastro-intestinal fistulas of sufficient magnitude to require special nutritional management. Eleven of these patients were transferred from other hospitals for treatment of their fistulas. There were 34 male and 22 female patients with ages ranging from 16 to 88 years (average 55 years). The distribution of the fistulas is shown in *Table I*.

Table I: SITES OF ORIGIN OF FISTULAS

Origin	Group I* July 1969– Dec. 1973 (54 mth)	Group II† July 1965– July 1969 (48 mth)
Oesophageal and oesophagogastric	7	7
Gastric	4	1
Gastroduodenal	2	—
Gastrojejunal	3	—
Duodenal	5	3
Pancreatic	8	1
Biliary	3	1
Jejunal	8	5
Ileal	6	7
Ileocolic and caecal	8	—
Colic	11	7
Total	65	32

* Includes 11 patients transferred from other hospitals for treatment of postoperative fistulas.
† Group studied retrospectively.

Group II

This group consisted of 30 patients with 32 fistulas. As the review of group II was retrospective (group I was a prospective study) only patients whose fistulas had been recorded in the diagnosis, operation notes or as complications could be included (*Table I*). There were 16 male and 14 female patients with ages ranging from 29 to 89 years (average 54 years).

Methods of nutritional support

Routine intravenous feeding solutions contain 5 per cent dextrose, and 3 litres/day would provide 510 kcal, which would have a protein-sparing effect and decrease catabolism by 50 per cent (Gamble, 1958). However, for anabolism and healing in these patients the energy requirements are much greater. Nutritional support was administered by one or a combination of the following methods (*Table II*).

Method I. Intravenous hyperalimentation: Patients received 2000–3000 non-protein kcal/day together with 80–175 g of fortified protein hydrolysate (Deitel, 1973; Deitel et al., 1973). This was infused

---

* Department of Surgery, University of Toronto and St Joseph's Hospital, Toronto.

Table II: MODES OF NUTRITION

Method:	No. of patients:
Intravenous hyperalimentation	55*
The lipid system	7
Elemental diet	30

* Combined with the other methods during treatment in 31 patients.

continuously via a catheter situated in a large *central* vein (Deitel and McIntyre, 1971) inserted by subclavian puncture. A small constant infusion pump was used to give a flow rate of about 500 mg of dextrose/min (100 mg of protein hydrolysate/min). Strict aseptic precautions were maintained during catheter insertion and dressing changes. Blood was drawn thrice weekly to monitor electrolytes, blood urea nitrogen and blood sugar. This method was used in 55 patients—alone in 24 patients and followed by one of the other two methods in 31 patients.

Method II. The lipid system: Using separate intravenous lines united to a terminal Y-connector attached to a needle in a *peripheral* vein (Deitel and Kaminsky, 1974; Deitel and Syed, 1974) 3 g/kg body weight 24 hr^{-1} of a 10 per cent soybean oil–egg yolk phospholipid–glycerol emulsion (Intralipid) was infused simultaneously with 5 per cent protein hydrolysate in 5 per cent dextrose (*Fig.* 1). The iso-osmolal Intralipid prevented phlebitis in the peripheral vein which may be caused by the hyperosmolal protein hydrolysate-dextrose solution. Electrolytes, vitamins and heparin were added to the protein hydrolysate–dextrose solution. Using this method the patient received more than 2000 non-protein kcal/day and 100–150 g of amino acid. Advantages of this method are that the complications of caval catheters are avoided and hyperosmolar coma does not occur; disadvantages are that the flow rate must be adjusted frequently and forearm movement is limited. The lipid system was used in 7 patients, in sequence with intravenous hyperalimentation and/or elemental diets.

Method III. Elemental diets: These are nutritionally complete, predigested, bulk-free, liquid diets containing simple sugars and properly balanced amino acids requiring no significant digestion by enzymes (Deitel and Kaminsky, 1974; Deitel and Syed, 1974). All essential vitamins, electrolytes and trace minerals are present, as well as ethyl linoleate as a source of essential fat. These diets contain the necessary energy for protein synthesis—more than 150 non-protein kcal/g of nitrogen provided (Moore, 1959). When flavours were accepted orally, the diet was taken as frequent sips to prevent cramping and diarrhoea, and water by mouth was taken *ad libitum* to prevent hypertonic dehydration. When not accepted orally, the diet was delivered via a No. 8 nasogastric tube with a constant infusion pump, with the head of the bed elevated to obviate aspiration. Occasionally the diet was given by a gastrostomy or jejunostomy tube. Elemental diets were used in 30 patients—in sequence with intravenous hyperalimentation and/or the lipid system in 28.

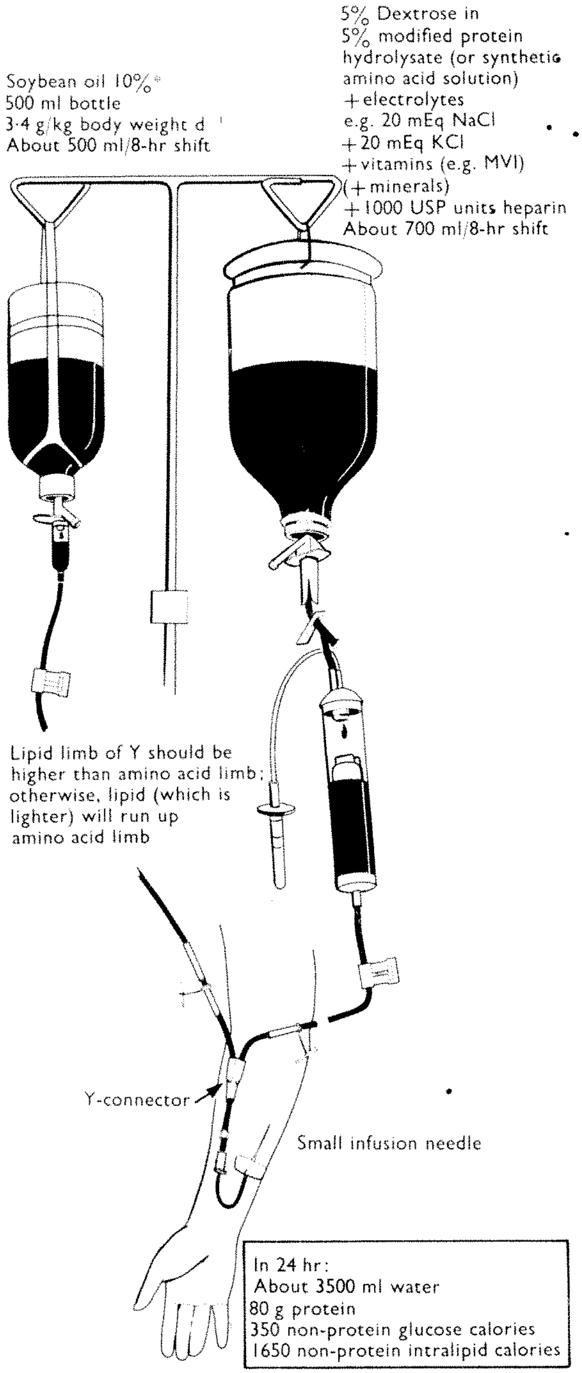


Fig. 1. The lipid system as applied to a 50-kg nutritionally depleted patient. *Intralipid (1·1 Cal/ml for a 10 per cent solution).

Results

Group I

Fifty-two of the 65 fistulas (80 per cent) closed spontaneously with nutritional support (*Table III*). Operative closure was necessary for 7 fistulas (10·8 per cent) in 6 patients, two attempts being

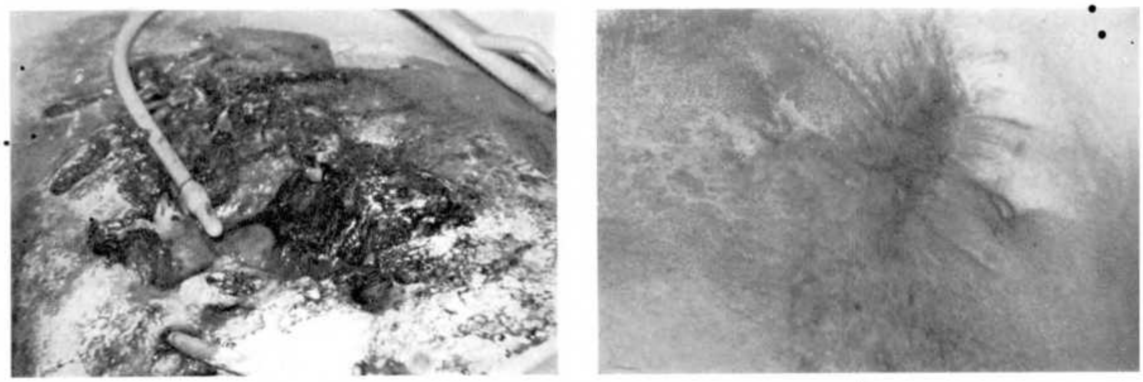


Fig. 2. *a*, Extensive abdominal wall defect with enterocutaneous fistulas. Risk was prohibitive. *b*, Healing achieved through sequential treatment with intravenous hyperalimentation, lipid system and elemental diet.

Table III: RESULTS OF TREATMENT

Group	No. of fistulas	Spontaneous closure		Attempted operative closure		Successful operative closure	Overall successful closure		Average duration of treatment in survivors (d)	Mortality	
		No.	%	No.	%		No.	%		No.	%
I	65 in 56 patients	52 in 45 patients*	80	7 in 6 patients	10·8	4 in 4 patients	56 fistulas	86·2	44·7	7	12
II	32 in 30 patients	11 in 11 patients	34·4	10 in 9 patients	31·3	8 in 7 patients	19 fistulas	59·4	79·8	12	40

* In 2 patients, spontaneous closure of jejunal fistulas occurred successfully after more than 200 days.

Table IV: MORTALITY IN SERIES REPORTED IN THE LITERATURE

Author	Dates	No. of fistulas	Mortality (%)
Edmunds et al. (1960)	1946–59	157	44
Chapman et al. (1964)	1953–63	56	45
Halversen et al. (1969)	1945–69	55	40
Lorenzo and Beal (1969)	1959–68	18	40
Voitk et al. (1973)	Not stated	36	28
MacFadyen et al. (1973)	1970–72	78	6·45
Present series (1974)	1. 1965–69	32	40
	2. 1969–73	65	12·5

unsuccessful with the ultimate death of the patient. The overall closure rate was 86·2 per cent.

The average duration of treatment in the survivors from the time nutritional support was instituted to the time of fistula closure was 44·7 days. Jejunal fistulas took longest to close—more than 200 days in 2 patients, operation being impossible in both (*Fig.* 2).

Seven patients died, giving an overall mortality of 12·5 per cent. Five of the 7 deaths occurred in patients with disseminated carcinoma, which was undiagnosed at the time of commencing nutritional support. If these cases of carcinomatosis, who should not have been managed thus, are excluded the overall mortality was 3·6 per cent.

Group II

Spontaneous closure occurred in 11 of 32 fistulas (34·4 per cent). Operative closure was undertaken for 10 fistulas (31·3 per cent) in 9 patients and was unsuccessful in 2, resulting in the death of the patients. The overall fistula closure rate was 59·4 per cent. The average duration of treatment in the survivors was 79·8 days. Twelve deaths occurre giving a mortality rate of 40 per cent.

Discussion

The recent introduction of nutritional methods h reduced the high mortality and morbidity associat with external gastro-intestinal fistulas (*Table I* Although we emphasize the importance of nutritio an aggressive policy towards control of the fistula ar associated sepsis was also pursued. This includ the introduction into the fistula of a catheter attach to effective suction to prevent pooling. The suctic catheter was slowly withdrawn and replaced by narrower catheter. This resulted in closure of t fistula or the formation of a well-defined tract ov which an ileostomy bag could be applied. Occasional the patient was placed prone on a Stryker bed afford free drainage and to prevent skin digestion.

The surrounding skin was protected with kara gum powder, karaya and glycerin, aluminium past tincture of benzoin, or cod liver oil–zinc oxide cor pound barrier cream (Desitin). In our experien a liberal amount of the latter cream was the mo effective, as the enzyme-rich fluid flowed over t cream without digesting the underlying skin. The debilitated patients were placed on pulsating a mattresses to avoid decubitus ulcers and mobilized much as possible to promote anabolism. Generaliz sepsis was controlled with the appropriate antibiotic and localized abscesses were drained when diagnose

Factors which contributed to prolonged fistu drainage were: (1) distal bowel obstruction, ir tability, inflammation or abscess; (2) previo irradiation to the area; (3) underlying granulomato bowel disease; (4) bowel immediately adjacent to skin with a very short fistulous tract; (5) metallic mercury (from ruptured balloon of a long intestinal tube) in the fistulous tract; (6) reactive foreign bodies, e.g. heavy silk sutures. The fistula could often be outlined radiographically on liquid contrast-medium gastro-intestinal studies. However, the introduction of radio-opaque liquid into the external opening of the fistula was the most successful way of identifying its nature and origin. Conservative treatment was abandoned and operative closure performed with distal obstruction, wide breakdown or complete disruption of an anastomosis.

Most fistulas were treated initially with intravenous hyperalimentation, while electrolyte and fluid balances were restored. At the same time adequate calories and amino acids for protein synthesis were supplied, while suppression of gastro-intestinal secretions (Hamilton et al., 1971) caused a rapid decrease in fistula output. Those who eventually required surgery were in a better nutritional state to withstand operation. Only one patient developed catheter sepsis (*Staphylococcus aureus*), which resolved immediately on removal of the catheter (Sanderson and Deitel, 1973). Another patient developed non-ketotic hyperosmolal coma (Deitel et al., 1973; Sanderson and Deitel, 1974), which was treated with insulin and rehydration without ill effect to the patient. No patient died from the nutritional treatment.

Although fistulas often heal more rapidly on intravenous hyperalimentation than on elemental diets, many potential dangers of the former are removed by changing to elemental diets when fistulas are close to being solidly healed. In situations where intravenous hyperalimentation is difficult to institute, e.g. the proximity of a burn scar or a tracheostomy, the peripheral lipid system is valuable.

Acknowledgement

We thank St. Joseph's Hospital (Toronto) Research Foundation for financial support.

References

BACON H. E. and GENNARO A. R. (1969) The diagnosis and management of intestinal fistulas. *Dis. Colon Rectum* **12**, 7–12.

CHAPMAN R., FORAN R. and DUNPHY J. E. (1964) Managements of intestinal fistulas. *Am. J. Surg.* **108**, 157–164.

DEITEL M. (1973) Intravenous hyperalimentation. *Can. Nurse* **69**, 38–44.

DEITEL M. and KAMINSKY V. M. (1974) Total nutrition by peripheral vein—the lipid system. *Can. Med. Assoc. J.* **11**, 152–154.

DEITEL M. and MCINTYRE J. A. (1971) Radiographic confirmation of site of central venous pressure catheters. *Can. J. Surg.* **14**, 42–52.

DEITEL M., SANDERSON I. and PETSOULAS T. (1973) A system of intravenous hyperalimentation. *Int. Surg.* **58**, 670–675.

DEITEL M. and SYED A. K. (1974) Elemental diets in management of clinical nutritional problems. *Mod. Med. Can.* **29**, 471–475.

DUDRICK S. J., WILMORE D. W., VARS H. M. and RHOADS J. E. (1968) Long-term total parenteral nutrition with growth, development, and positive nitrogen balance. *Surgery* **64**, 134–142.

EDMUNDS L. H., WILLIAMS G. M. and WELCH C. E. (1960) External fistulas arising from the gastro-intestinal tract. *Ann. Surg.* **152**, 445–471.

GAMBLE J. L. (1958) *Chemical Anatomy, Physiology and Pathology of Extracellular Fluid.* Cambridge, Mass., Harvard University Press.

HALVERSEN R. C., HOGLE H. H. and RICHARDS R. C. (1969) Gastric and small bowel fistulas. *Am. J. Surg.* **118**, 968–972.

HAMILTON R. F., DAVIS W. C., STEPHENSON D. V. and MAGEE D. F. (1971) Effects of parenteral hyperalimentation on upper gastrointestinal tract secretions. *Arch. Surg.* **102**, 348–352.

LORENZO G. A. and BEAL J. M. (1969) Management of external small bowel fistulas. *Arch. Surg.* **99**, 394–396.

MACFADYEN B. V., DUDRICK S. J. and RUBERG R. L. (1973) Management of gastrointestinal fistulas with parenteral hyperalimentation. *Surgery* **74**, 100–105.

MOORE F. D. (1959) *Metabolic Care of the Surgical Patient.* Philadelphia, Saunders.

SANDERSON I. and DEITEL M. (1973) Intravenous hyperalimentation without sepsis. *Surg. Gynecol. Obstet.* **136**, 577–585.

SANDERSON I. and DEITEL M. (1974) Insulin response in patients receiving concentrated infusions of glucose and casein hydrolysate for complete parenteral nutrition. *Ann. Surg.* **179**, 387–394.

VOITK A. J., ECHAVE V., BROWN R. A., MCARDLE A. H. and GURD E. N. (1973) Elemental diet in the treatment of fistulas of the alimentary tract. *Surg. Gynecol. Obstet.* **137**, 68–72.

Br. J. Surg. Vol. 62 (1975) 104–107

The treatment of resistant malignant ascites by insertion of a peritoneo-atrial Holter valve

A. V. POLLOCK*

SUMMARY

Holter valves have been used in 9 cases to drain ascites, and in 1 case a pleural effusion, into the superior vena cava. All these effusions were due to malignant disease. Three patients died before the results of the operation could be assessed and in 1 case ascites rapidly recurred. Five patients were relieved until death from their primary disease. One patient died 3½ years after insertion of the valve, but ascites had returned—probably as a result of recurrent blockage of the valve by particulate matter.

THE formation of ascites (like that of tissue fluid) depends on the balance of hydrostatic and osmotic pressures between capillaries, tissue spaces and the peritoneal cavity, the effective functioning of capillary and peritoneal semipermeable membranes and the free flow of lymph.

The commonest causes in the United Kingdom are cirrhosis of the liver and secondary carcinoma of the peritoneum. Non-operative treatment may eliminate the ascites in both conditions, but paracentesis may be needed and, if repeated, causes distress to the patient and depletion of protein.

During the past 3 years the author has operated on 10 patients whose malignant effusions were resistant to orthodox treatment, placing a Holter valve subcutaneously between the peritoneal (9 cases) or pleural (1 case) cavities and the superior vena cava or right atrium. The pressure differential is sufficient to ensure a continuous centripetal flow of fluid without manipulation of the valve.

Methods

The only indication for operation is the resistance of ascites to conservative treatment, and the result is that many patients are operated on at a terminal stage of their disease. As a rule, light general anaesthesia is used, but one valve was inserted under local infiltration anaesthesia.

The patient is placed supine on the operating table with his arms by his sides. A 3-cm incision is made just below the tip of the ninth rib and deepened to the peritoneum, which is punctured and ascitic fluid aspirated. (Early in the series all the fluid was not removed, and as a result 1 patient developed hypervolaemic heart failure and another suffered a massive leak of ascitic fluid into the subcutaneous tissues.)

The inlet tube of a low-pressure Holter valve is placed in the peritoneal cavity and the abdominal wall sutured around it. The valve and the outlet tube are connected and the valve positioned over a convenient rib, which allows detection of patency postoperatively. A new incision 5 cm long is made below the outer half of the clavicle on the same side. The pectoralis major muscle is split and divided and the pectoralis minor divided to give access to the first and second parts of the axillary vein. A pair of sigmoidoscopic biopsy forceps is thrust subcutaneously from the upper to the lower incision and the outlet tube of the valve drawn into the upper wound. The cephalic vein is opened near its junction with the axillary vein and the tube manipulated through this opening into the axillary vein, subclavian vein and superior vena cava until the tip lies opposite the right atrium. Its position is verified radiographically and the wounds closed.

During the first few postoperative days diuretics are given in large doses, as fluid overloading is common.

Results (*Table I*)

The patient operated on for a massive malignant pleural effusion due to carcinoma of the breast (*Case* 1) was relieved of the effusion, but died of carcinomatosis after a month.

The remaining 9 patients (*Cases* 2–10) had peritoneal carcinoma, the primary growths being in the breast (2), stomach (1), pancreas (1), ovary (2), bladder (1) and unknown (2).

The ascites of 8 of these 9 patients was temporarily relieved by operation. The ninth patient (*Case* 9) was *in extremis* and his ascites had rapidly reaccumulated after two paracenteses. The valve was inserted in the usual way but failed to function, and X-rays showed the tip of the outlet tube lying in the right ventricle (operative X-rays had been omitted in this case). The outlet tube was therefore shortened by 6 cm and the system functioned. He died in coma 2 days later and at autopsy the valve was patent.

Of the remaining 8 patients, 3 died of malignant disease within 28 days of insertion of the valve, 3 died between 1 and 5 months postoperatively without reaccumulation of the ascites, 1 died 4 months later with recurrent ascites and 1 patient died 3½ years after operation with recurrent ascites (*Case* 2).

Case report

Case 2: In July 1968 Mrs M. G., aged 51 years, had a left extended simple mastectomy for scirrhous carcinoma with involved axillary nodes. In 1969 skin nodules were found on the abdomen and back. Biopsy of one of these showed spheroidal celled carcinoma, and X-rays revealed disseminated

---

* Scarborough Hospital, Scarborough, Yorkshire.

Table I: DETAILS OF THE PATIENTS IN THE PRESENT SERIES

Case	Sex	Age (yr)	Primary disease	Previous treatment	Preoperative paracentesis intervals	Result of operation	Complications	Length of survival
1	F	46	Carcinoma of breast (right pleural effusion)	Radiotherapy Hypophysectomy	1 wk	Effusion cleared	Nil	4 wk
2	F	53	Carcinoma of breast	Mastectomy	2 wk	Ascites cleared	Temporary anasarca. Valve occluded at 27 months—reoperation	39 mth
3	F	54	Carcinoma of breast	Mastectomy Adrenalectomy	4 wk	Ascites cleared	Nil	19 wk
4	F	69	Carcinoma of ovary	Oophorectomy	1 wk	Ascites cleared	Anasarca	6 wk
5	F	81	Carcinoma of unknown origin	Paracentesis Intraperitoneal thiotepa Cyclophosphamide	4 wk	Ascites cleared	Nil	8 wk
6	M	41	Carcinoma of bladder	Total cystectomy	2 wk	Ascites cleared	Terminal cachexia	2 wk
7	M	67	Carcinoma of stomach	Total gastrectomy	1 wk	Died before assessment	Anasarca. Terminal cachexia	4 d
8	M	50	Carcinoma of unknown origin	Nil	1 wk	Died before assessment	Terminal cachexia	3 d
9	M	53	Carcinoma of pancreas	Nil	1 wk	Valve failed to function until outlet tube shortened	Terminal cachexia	9 d
10	F	58	Carcinoma of ovary	Paracentesis Intraperitoneal thiotepa Cyclophosphamide	6 wk	Ascites reaccumulated	Nil	17 wk

Table II: TREATMENT OF ASCITES

Principle	Non-operative treatment	Operative treatment
Prevention of formation	Diet: Avoidance of alcohol (C) Intraperitoneal cytotoxic drugs (M)	Reduction of portal pressure (C) Talma–Morrison omentopexy Side-to-side portacaval shunt Splenorenal shunt
Removal of fluid		Paracentesis abdominis (C and M) Peritoneo-ureteric anastomosis (C and M) Peritoneovesical anastomosis (C and M)
Absorption of fluid	Diuretics (C)	Intravenous infusion of fluid removed (C and M) Peritoneosaphenous anastomosis (C and M) Lymphovenous anastomosis (C) By producing a fistula into the subcutaneous tissues (C and M) By producing a fistula into the pleural cavity (C and M) Peritoneo-atrial shunt by Holter valve (C and M)

C, Cirrhotic. M, Malignant.

sclerotic bone metastases. Endocrine surgery was contemplated, but the patient's general health was so good that this was not advised. She continued symptom-free until December 1970 when she developed oedema of the ankles, followed by ascites. She felt ill and, for the first time, was unable to go about her normal affairs.

Following paracentesis in January 1971 the ascites reaccumulated within 2 weeks despite large doses of frusemide. A peritoneo-atrial Holter valve was therefore inserted in February 1971. Postoperatively she had a massive diuresis and lost 6 kg in weight.

She maintained good health for over 2 years, when ascites recurred. Chest X-ray showed no abnormality apart from sclerotic metastases in the ribs.

Under general anaesthesia the fluid was drained from the peritoneal cavity and the valve removed, leaving patent inlet and outlet tubes in position. The valve itself was found to be blocked at its entrance by a minute piece of white tissue. This was cleared out with a needle and the valve reinserted, but it failed to function and ascites reappeared within a month. A new valve was put in, but again blocked within a month. Periodic paracentesis was continued until the patient's death 3¼ years after insertion of the valve. Autopsy showed no pulmonary metastases.

Discussion (*Table II*)

Most cases of cirrhotic ascites can be controlled by a strict regimen of diuretics, sodium restriction, high protein diet and avoidance of alcohol. Sherlock (1971) reported 112 cirrhotic patients and failed to control ascites in only 6, none of whom survived a year.

Malignant ascites, on the other hand, responds poorly to treatment. Cytotoxic drugs (MacGregor et al., 1969), radiotherapy, hormones and endocrine surgery have not always been successful. Many patients are condemned to repeated paracenteses which deplete albumin reserves and have a demoralizing and weakening effect. This is particularly true of those with disseminated carcinoma of the breast who may live for several years after the development of ascites.

Many methods of surgical relief of cirrhotic ascites have been described (Crosby and Cooney, 1946; Welch et al., 1964; Fish et al., 1968; Schreiber et al., 1968; Steigmann et al., 1968; Hermann and Taylor, 1971; Sein, 1973; Parbhoo et al., 1974), but surgical treatment of malignant ascites has attracted less attention.

Ferguson (1943) removed the left kidney and anastomosed the renal pelvis to the peritoneum, and Mulvany (1955) treated 7 patients with malignant and 3 with cirrhotic ascites by draining the peritoneal cavity into the bladder. The problem of protein loss was not solved by these operations.

Many operations have been designed to drain ascitic fluid into the general circulation. In 1907 Ruotte successfully anastomosed the divided proximal end of the long saphenous vein to the peritoneum in the lower abdomen so that ascitic fluid drained into the femoral vein. Unfortunately, later workers found that the anastomosis closed and the saphenous vein clotted. Schnee (1955) sought to overcome this difficulty by using a 'button' which traversed the abdominal wall and on to which he tied the saphenous vein.

Crosby and Cooney (1946) recorded 6 patients with ascites (5 cirrhotic and 1 due to constrictive pericarditis) treated by insertion of a glass tube or 'button' to lead ascitic fluid through the anterior abdominal wall into the subcutaneous tissues whence it was absorbed. One patient died of peritonitis, but the other 5 were relieved of their ascites. El-Toraei (1961) reported 18 patients whose cirrhotic ascites was treated by the construction of a pleuroperitoneal fistula. Three died postoperatively and 3 were 'cured', but a pleural effusion remained in all the cases.

In 1962 Smith published a preliminary communication on the use of a Spitz–Holter valve in a patient who had been subjected to numerous paracenteses for resistant cirrhotic ascites. The inlet tube of the valve was inserted into the peritoneal cavity, the valve lay in the subcutaneous tissue over the symphysis pubis and the outlet tube was passed into the long saphenous vein and thence to the inferior vena cava. Six months later the patient was well.

Experience of the 10 cases described in this paper leads the author to believe that malignant ascites can usually be controlled in the same way as hydrocephalus by draining the fluid through a one-way valve into a central vein. The operation has not previously been used for the palliative treatment of malignant ascites, possibly because of the fear of dissemination of cancer cells into the general circulation. However, the improvement in the health of *Case* 2 following insertion of the valve, together with the absence of lung metastases more than 3 years later, makes this a doubtful objection.

A more valid criticism of the method is the possibility that the valve will become obstructed by particulate matter in the ascitic fluid. This is thought to be the cause of the late failure in *Case* 2 and the complete failure in *Case* 10, when the ascitic fluid reaccumulated within a month of insertion of a valve. The latter patient died 3 months later and examination showed that the peritoneal inlet tube was not only blocked by a small plug of fibrin and cancer cells but also acutely kinked. In future a reservoir valve of the Pudenz type instead of the classic Holter valve will be used.

Most of the patients reported here were at a terminal stage of their disease, and 4 of them did not live long enough to benefit from the relief of their ascites. The operation does, however, have a place in the management of cancer patients whose end would otherwise be made more miserable by rapid reaccumulation of fluid.

References

CROSBY R. and COONEY E. A. (1946) Surgical treatment of ascites. *New Engl. J. Med.* **235**, 581–585.

EL-TORAEI I. (1961) Surgical treatment of cirrhotic ascites with a new operation (pleuroperitoneostomy). *J. Int. Coll. Surg.* **35**, 436–445.

FERGUSON C. (1943) Ascites: an operation for its relief. A case report. *J. Urol.* **50**, 164–168.

FISH J. C., SARLES H. E., REMMERS A. R. and WILLIAMS R. D. (1968) Effect of thoracic duct decompression on ascites. *JAMA* **203**, 98–102.

HERMANN R. E. and TAYLOR P. C. (1971) The results of selection of patients for portal systemic shunt. *Surg. Gynecol. Obstet.* **133**, 1008–1012.

MACGREGOR A. B., MACLEOD D. A. D. and THOMSON J. W. W. (1969) Combined chemotherapy in the treatment of malignant effusions. *Br. J. Surg.* **56**, 489–491.

MULVANY D. (1955) Vesico-coelomic drainage for the relief of ascites. *Lancet* **2**, 747–749.

PARBHOO S. P., AJDUKIEWICZ A. and SHERLOCK S. (1974) Treatment of ascites by continuous ultrafiltration and reinfusion of protein concentrate. *Lancet* **1**, 949–952.

RUOTTE M. (1907) Abouchement de la veine saphène externe au péritoine pour resorber les épanchements sciatiques. *Lyon Méd.* **109**, 574–577.

SCHNEE, C. F. (1955) Surgical treatment of abdominal ascites due to cirrhosis of the liver. Preliminary experience with new cannula button in peritoneosaphenous anastomosis. *J. Int. Coll. Surg.* **16**, 199–207.

SCHREIBER H. W., KOCH W., VON ACKEREN H., GEORGI TH. and SCHILLING K. (1968) Cervical lymphovenous anastomosis for portal hypertension in cirrhosis of the liver. *Ger. Med. Mon.* **13**, 361–366.

SEIN M. M. (1973) Cervical lymphovenous shunt in intractable ascites—a clinical study. *Br. J. Surg.* **60**, 900.

SHERLOCK S. (1971) *Diseases of the Liver and Biliary System*, 4th ed. (rev. 3rd ptg). Oxford, Blackwell, pp. 144–158.

SMITH A. N. (1962) Peritoneo-caval shunt with a Holter valve in the treatment of ascites. *Lancet* **1**, 671–672.

STEIGMANN F., LONG D. and MEJICANO R. (1968) Lymphatic decompression therapy of 'intractable' ascites. *Am. J. Gastroenterol.* **50**, 47–54.

WELCH H. F., WELCH C. S. and CARTER J. H. (1964) Prognosis after surgical treatment of ascites: results of side-to-side shunt in 40 patients. *Surgery* **56**, 75–82.

Br. J. Surg. Vol. 62 (1975) 108–112

Abdominal approach for the ligation of bleeding oesophageal varices

STANLEY S. MILLER*

SUMMARY

The conventional surgical treatment of bleeding oesophageal varices in the emergency situation is based upon the Boerema-Crile operation of transthoracic oesophagotomy and ligation of the varices. This and the other methods of treatment of this condition in current practice are discussed.

Two cases are reported in which a transabdominal oesophagogastrotomy was used to approach the site of bleeding. This operation is described and the theoretical and practical advantages it appears to offer over the standard approach are considered.

EMERGENCY surgery to stop bleeding from oesophageal varices carries a high mortality, but death is almost inevitable if bleeding is allowed to continue. The mortality of a single bleed from oesophageal varices has been reported as over 50 per cent (Garceau et al., 1963). Of the survivors from this initial haemorrhage, 50 per cent will die within 1 year from further massive bleeding (McDermott, 1972). If bleeding persists or recurs despite adequate conservative measures it has been advocated that direct control be achieved by transthoracic oesophagotomy and ligation of the varices (Boerema, 1949; Crile, 1953; Linton and Warren, 1953) (*Fig.* 1). The mortality and morbidity of this operation, however, remain high because these are poor risk patients, often desperately ill.

In a series of 58 patients treated by the Boerema–Crile operation reported by Rothwell-Jackson and Hunt (1971) there were 25 early postoperative deaths and 13 late deaths. It was thought, however, that, since most if not all of these patients would have died without surgery, 'it is not unreasonable to consider the results of surgery in these circumstances in terms of salvage (29 per cent) rather than mortality'.

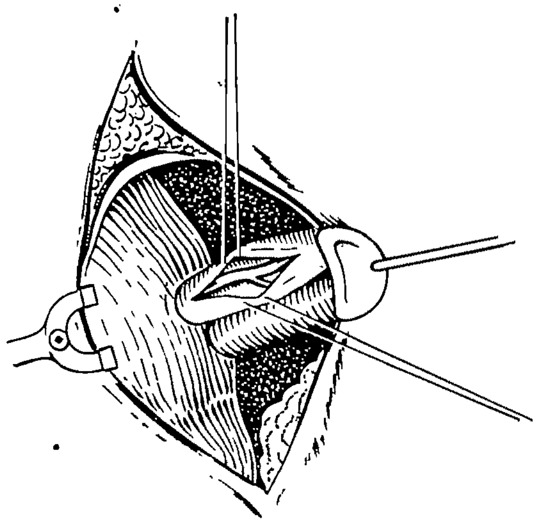


Fig. 1. Transthoracic ligation of oesophageal varices.

In the 2 cases reported here direct ligation of bleeding oesophageal varices by transabdominal oesophagogastrotomy was performed. This proved to be a safe practical method of approaching the bleeding source and to have certain advantages over the normal transthoracic operation.

Case reports

Case 1: E. F. a male aged 44 years. In May 1972 when this man was investigated for anaemia due to gastro-intestinal bleeding, a duodenal ulcer was demonstrated radiologically. It was also noted that there was distortion of the fundal mucosal pattern, suggestive of varices, although it was considered that a similar appearance could be produced by hypersecretory gastric mucosa. Endoscopy revealed hypertrophic gastritis but no convincing evidence of varices. Liver biopsy, however, showed the features of a micro-nodular cirrhosis. He was also found to be hypertensive and diabetic.

The patient remained well until emergency admission in November 1972 with a small haematemesis. Although initially stable, shortly after admission he suddenly vomited several pints of fresh blood and had a severe hypotensive episode. It seemed clear that urgent surgical intervention was indicated, and following a short period of preoperative preparation a laparotomy was performed.

An abdominal approach was selected because of the possibility that the source of bleeding was from a posterior duodenal ulcer. In view of the continuing haemorrhage and the previous equivocal findings it was considered that endoscopy might only produce further delay without necessarily contributing to the diagnosis.

At operation the presence of cirrhosis was confirmed but the source of bleeding was not immediately apparent. A small distal gastrotomy was thus made and through this, active bleeding was seen to be coming from the upper part of the lesser curve, the duodenum being clear. As the source seemed certain to be variceal a separate oesophagogastrotomy was fashioned (*Fig.* 2). This was facilitated by dividing the peritoneum and hiatal membrane over the abdominal part of the oesophagus and with finger dissection bringing the lower thoracic oesophagus into the abdomen. A portion of Paul's tubing was passed around the oesophagus to act as a retractor, as when performing a truncal vagotomy. The triangular ligament was not divided as it is felt that the left lobe of the liver is more easily managed if fixed by this structure and lifted upwards with a large Dyball retractor.

The peri-oesophageal veins were transected and, on opening the oesophagogastric junction between stay sutures, the source of bleeding was found to be a varix on the lesser curve aspect of the cardia. This and two other columns of varices were obliterated by running silk sutures, commencing on the gastric fundus and extending 7–8 cm up the oesophagus. This was facilitated by holding the margins of the incision open with

---

* Department of Surgery, University of Aberdeen.

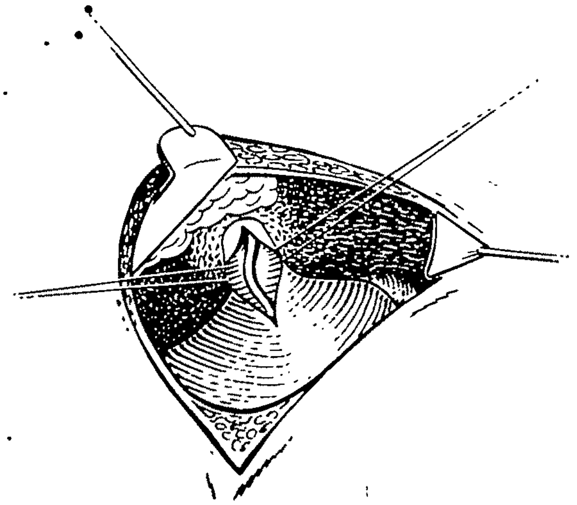


Fig. 2. Transabdominal ligation of oesophagogastric varices.

light tissue forceps. When the bleeding was satisfactorily under control the incision was closed with inner continuous chromic catgut and interrupted seromuscular silk sutures. The original gastrotomy incision was closed in a similar manner.

At the completion of the procedure a noxytiolin washout of the peritoneal cavity was performed. It has been our practice to do this after operations on all forms of acute gastroduodenal haemorrhage, as the site of operation inevitably becomes contaminated with blood clot which may have been in an achlorhydric stomach for several days and mixed with swallowed saliva. The abdomen was then closed in layers with catgut, nylon deep tension sutures and peritoneal drainage.

The patient made an uncomplicated postoperative recovery except for an early period of confusion which was attributed to ammonia absorption from the blood in the bowel. A Gastrografin swallow and meal showed no leakage and the chest X-ray remained clear throughout. He is well now 1 year after operation and is being considered for a portacaval shunt.

In this case an abdominal incision was chosen because of the possibility that the source of bleeding was in the duodenum. When the bleeding was found to arise from oesophageal varices little difficulty was encountered in approaching the lower end of the oesophagus in this way and good exposure was obtained.

Case 2: H. M., a female aged 54 years with no previous medical history, was admitted with a 24-hour history of haematemesis following the ingestion of aspirin. There was little of note on examination or investigation except for a haemoglobin level of 5·49 g per cent. The blood loss was restored with 6 units of blood overnight and at first there was apparently complete stabilization. However, a large fresh haematemesis the next morning led to urgent laparotomy. This was carried out via a paramedian incision and oesophageal varices were found, one of which was bleeding at the level of the cardia. The haemorrhage was controlled and the varices obliterated through an oesophagogastrotomy, as described in *Case* 1. On this occasion a vagotomy was performed in order to mobilize the oesophagus further into the abdomen. Histological examination of a liver biopsy revealed primary biliary cirrhosis, a diagnosis which was supported by a positive anti-mitochondrial antibody test and a raised serum IgM level.

The patient made an uncomplicated postoperative recovery and remains well now 6 months after operation.

In this case there was haemorrhage to a degree requiring operation but no definitive preoperative diagnosis. An oesophagoscopy could have been used prior to exploration but experience with *Case* 1 gave confidence that if bleeding varices were encountered then control could be achieved from below. This in fact proved to be the case.

Transabdominal oesophagogastrotomy versus transthoracic oesophagotomy

There are several theoretical and practical reasons why transabdominal oesophagogastrotomy may give better results than transthoracic oesophagotomy.

1. *Oesophageal disruption*

In the transthoracic approach the oesophagus is incised at its weakest part. In spontaneous rupture of the oesophagus the tear, longitudinal and 1–8 cm in length, is most often on the left side just above the diaphragm. This coincides with the incision described in the Boerema–Crile operation. It is generally regarded that at this point the oesophagus is intrinsically weak and has least support from surrounding tissues. This view is reinforced by the fact that while there has been only one reported case of spontaneous rupture of the abdominal oesophagus (Strauch and Lynch, 1965) there are well over 100 involving the lower thoracic oesophagus (Tesler and Eisenberg, 1963).

The inherent weakness at this point together with other factors, such as delay in wound healing, may contribute to the disruptions which occur following the Boerema–Crile procedure. Oesophageal disruption was a major postoperative problem in the series presented by Rothwell-Jackson and Hunt in 1971. Of 58 transthoracic oesophagotomies, in 10 there was breakdown of the oesophagotomy incision and none of these patients survived.

2. *Morbidity of a thoracotomy*

These operations are carried out as emergencies on unprepared patients, often with pre-existent chronic heart and lung disease. It seems probable that an abdominal incision might have a lower incidence of chest complications than a thoracotomy. In the series of Rothwell-Jackson and Hunt (1971) pneumonia was a cause of early and late postoperative deaths, and non-fatal complications included surgical emphysema, pleural effusion and haemothorax.

There are also advantages in the employment of approaches and techniques which are in day-to-day use. As most of these emergencies are dealt with by general surgeons a laparotomy would appear to be the most logical approach. Further, since the introduction of truncal vagotomy in the treatment of duodenal ulceration (Dragstedt et al., 1947), surgeons have become more familiar with the abdominal approach to the oesophageal hiatus.

3. *Coexistent gastroduodenal pathology*

Clarke et al. (1958) reported a frequency of associated cirrhosis and peptic ulceration as high as 25 per cent. In a study of patients dying from massive gastro-intestinal haemorrhage, Chalmers et al. (1952) found that 27 per cent with known liver disease bled to death from a cause other than oesophageal varices.

There is thus a strong likelihood of coexistent gastroduodenal disease, which if not the actual source of the acute haemorrhage may merit definitive treatment in its own right. Failure to do this will add to the list of postoperative complications. Recognizing the high incidence of peptic ulceration in cirrhotic patients, Rothwell-Jackson and Hunt (1971) latterly added thoracic vagotomy to the Boerema–Crile procedure, but there is little doubt that a laparotomy allows for a more complete assessment of the situation than does an approach through the chest. In their series there were early postoperative deaths from a perforated gastric ulcer, carcinoma of the stomach and a bleeding gastric varix. In Crile's original description of the technique used in 9 cases of variceal bleeding (Crile, 1953) there were 2 further episodes of bleeding. In 1 patient this originated from a gastric ulcer.

4. *Direction of flow and pressure in oesophageal varices*

The collateral route, provided by the oesophageal varices, is fed mainly from below by the vasa brevia and by reversal of flow in the left gastric vein. It seems rational to ligate the varicose vessels as close as possible to the source of high venous pressure. Thus, ligation in the oesophagus may leave gastric varices still exposed to a high venous pressure. If varices should be left at a higher level in the oesophagus after oesophagogastric ligation these are liable to be exposed to a low systemic venous pressure and thus unlikely to produce catastrophic haemorrhage. The level of the bleeding point is variously given in the literature but in most it is stated that it will be close to or below the cardia (Hunt, 1964; McDermott, 1972).

5. *Unknown source of bleeding*

The precise diagnosis of the source of upper gastrointestinal tract haemorrhage before operation can be often difficult and sometimes impossible. It may be necessary to explore patients when the diagnosis is still in question. Adoption of the transabdominal approach to oesophageal varices means that most contingencies will be covered by a laparotomy.

Discussion

Haemorrhage from oesophageal varices is invariably serious and often fatal. Death is either from exsanguination or the precipitation of hepatic failure. If the stress of a major emergency surgical procedure is added to the shock produced by massive haemorrhage, the likelihood of fatal hepatic decompensation is increased.

The mortality of emergency operation in the treatment of uncontrolled haemorrhage is very high. Thus, emergency portacaval anastomosis carries a mortality of 50–60 per cent (O'Sullivan and Payne, 1956; Wantz, 1957). Emergency gastric transection (Tanner, 1961) is a formidable operation and there is a high incidence of recurrent haemorrhage, so that it cannot be regarded as a definitive procedure (O'Donnell and Maloney, 1968). There are similar objections to emergency oesophageal transection, the operation of choice at the Royal Free Hospital. In a recent report from that hospital, George et al. (1973) noted an operative mortality rate of 53 per cent in patients with cirrhosis. To date, transthoracic ligation has been considered the best emergency procedure from the point of view of haemorrhage control, but this has a mortality of about 40 per cent (Rothwell-Jackson and Hunt, 1971).

Ideally, if haemorrhage could be controlled with surety by conservative means, liver function might be improved and an elective shunt procedure carried out in optimal conditions with more acceptable mortality figures. The importance of non-operative control of bleeding has been long recognized, but of the methods tried, none has been entirely satisfactory, including intravenous Pitressin (Shaldon and Sherlock, 1960), the Sengstaken tube (Vorrhees, 1959) and oesophagogastric cooling (Wangensteen et al., 1963). More encouraging results have recently been reported by the use of sclerosant injection therapy (Hunt et al., 1969). In 100 consecutive patients control was achieved in 90 per cent of cases with a mortality of less than 20 per cent. Others, however, have found visualization of the injection site difficult when the bleeding is profuse (Rothwell-Jackson and Hunt, 1968), and it can be difficult for the inexperienced.

The transabdominal route for the ligation of oesophageal varices was described in 1956 by Welch (1956), who used it in 5 patients with cirrhosis of the liver and bleeding, noting that control of haemorrhage was complete in all. Three patients died in liver failure and this he attributed to poor liver function and the lateness of surgery. In each of these 3 cases, haemorrhage was initially considered to have been controlled with the Sengstaken tube, but there was persistent or recurrent bleeding necessitating late surgical intervention.

Criticism of the transabdominal approach has mainly been that it can be difficult to negotiate an enlarged liver. In the cases reported here a large deep retractor was used to lift the liver away from the oesophagus. Welch (1956) divided the left triangular ligament and approached the oesophagus over the top of the left lobe of the liver, which was retracted downwards and to the right. Difficulty will also be encountered if attempts are made to perform a transgastric ligation of varices, and it should be emphasized that for easier and more effective control an oesophagogastrotomy incision must be made. Therefore if a diagnosis of a bleeding oesophageal varix is made through the initial small pylorotomy this should not be extended proximally but closed later as a pyloroplasty, and a separate incision made over the cardia. Vagotomy is indicated to facilitate mobilization of the lower oesophagus and because of the high incidence of peptic ulceration in cirrhosis. It also reduces gastric acidity which may be incriminated as a factor in recurrent variceal haemorrhage. Consequently it is felt that pyloroplasty should be added to this operation.

Choice of suture material

In the cases reported here non-absorbable suture material was used to obliterate the varices, although in most reported cases catgut has been advocated. There is some uncertainty from experimental work about the duration of integrity of catgut in the stomach (Howes, 1928; Holder, 1946), and our feeling has been that non-absorbable material provides a more certain method of ligation in the short term, accepting the possibility that a continuous stitch of this material may later cause symptoms of ulceration (Tanner, 1951). It may be that polyglycolic acid (Dexon) will prove to be a more satisfactory suture material in this situation and we are currently investigating this possibility.

Conclusions

Transabdominal oesophagogastrotomy and ligation is a sure method of haemorrhage control well within the competence of a general surgeon and, for the reasons outlined above, may have advantages over the transthoracic approach.

Once it is apparent that there is massive gastrointestinal haemorrhage the patient is best served by urgent operation with no time wasted on medical measures, which can be time-consuming and uncertain as far as the control of haemorrhage is concerned. Endoscopy is unnecessary if the transabdominal approach is chosen. Haemorrhage from oesophageal varices should be regarded in the same way as any other situation where there is massive bleeding.

The abdominal approach, we feel, offers a method of control which can be swiftly performed with a minimum of upset to the patient. Although our experience has been of only 2 cases we have been impressed by their smooth uncomplicated postoperative recovery. Like the transthoracic approach, however, it should not be regarded as a definitive procedure and the patient should probably be considered for a portacaval shunt on recovery.

Acknowledgements

I am grateful to Mr P. F. Jones for guidance in the management of these patients and to Professor G. Smith and Dr P. W. Brunt for helpful criticism in the preparation of this article. I thank Mr Nigel Lukins for the preparation of the illustrations.

References

BOEREMA I. (1949) Surgical therapy of bleeding varices of the oesophagus in cirrhosis of the liver and Banti's syndrome. *Arch. Chir. Neerl.* **93**, 4174–4182.

CHALMERS T. C., ZAMCHECK N., CURTINS G. W. and WHITE F. W. (1952) Fatal gastro-intestinal haemorrhage: clinicopathologic correlations in 101 patients. *Am. J. Clin. Pathol.* **22**, 634–645.

CLARKE J. S., OZERAN R. S., HART J. C., CRUZE K. and CREVLING V. (1958) Peptic ulcer following portacaval shunt. *Ann. Surg.* **148**, 551–566.

CRILE G. jun. (1953) Treatment of esophageal varices by transesophageal obliteration. *Surg. Gynecol. Obstet.* **96**, 573–576.

DRAGSTEDT C. R., HARPER P. V. jun., TOVEE E. B. and WOODWARD E. R. (1947) Section of the vagus nerves to the stomach in the treatment of peptic ulcer. *Ann. Surg.* **126**, 687–699.

GARCEAU A. J., CHALMERS T. C. and THE BOSTON INTERCITY GROUP (1963) The natural history of cirrhosis. 1. Survival with oesophageal varices. *New Engl. J. Med.* **268**, 469–473.

GEORGE P., BROWN C., RIDEWAY G., CROFTS B. and SHERLOCK S. (1973) Emergency oesophageal transection in uncontrolled variceal haemorrhage. *Br. J. Surg.* **60**, 635–640.

HOLDER E. J. (1946) Desirable factors in surgical sutures. PhD Thesis, Edinburgh.

HOWES E. L. (1928) Factors determining the loss of strength of catgut when embedded in tissue. *JAMA* **90**, 530–532.

HUNT A. H. (1964) Haematemesis in portal hypertension. *Br. J. Surg.* **51**, 749–752.

HUNT P. S., JOHNSTON G. W. and RODGERS H. W. (1969) The emergency management of bleeding oesophageal varices with sclerosing injections. *Br. J. Surg.* **56**, 305–307.

LINTON R. R. and WARREN R. (1953) The emergency treatment of massive bleeding from oesophageal varices by transoesophageal suture of these vessels at the time of acute haemorrhage. *Surgery* **33**, 243–255.

MCDERMOTT W. V. jun (1972) Liver and portal circulation. In: IRVINE W. T. (ed.) *Scientific Basis of Surgery*, 2nd ed. London, Churchill Livingstone, pp. 117–136.

O'DONNELL B. and MALONEY M. A. (1968) Development and course of extrahepatic portal obstruction in children. *Lancet* **1**, 789–791.

O'SULLIVAN W. D. and PAYNE M. A. (1956) The emergency portacaval shunt. *Surg. Gynecol. Obstet.* **102**, 668–676.

ROTHWELL-JACKSON R. L. and HUNT A. H. (1968) The surgical treatment of portal hypertension. *Br. J. Clin. Pract.* **22**, 156–168.

ROTHWELL-JACKSON R. L. and HUNT A. H. (1971) The results obtained with emergency surgery in the treatment of persistent haemorrhage from gastro-oesophageal varices in the cirrhotic patient. *Br. J. Surg.* **58**, 205–215.

SHALDON S. and SHERLOCK S. (1960) The use of vasopressin ('Pitressin') in the control of bleeding from oesophageal varices. *Lancet* **2**, 222–225.

STRAUCH G. O. and LYNCH R. E. (1965) Subphrenic extrathoracic rupture of the esophagus: first reported case. *Ann. Surg.* **161**, 213–217.

TANNER N. C. (1951) Operative methods in the treatment of peptic ulcer. *Edinb. Med. J.* **58**, 279–292.

TANNER N. C. (1961) The late results of porto-azygos disconnection in the treatment of bleeding from oesophageal varices. *Ann. R. Coll. Surg. Engl.* **28**, 153–174.

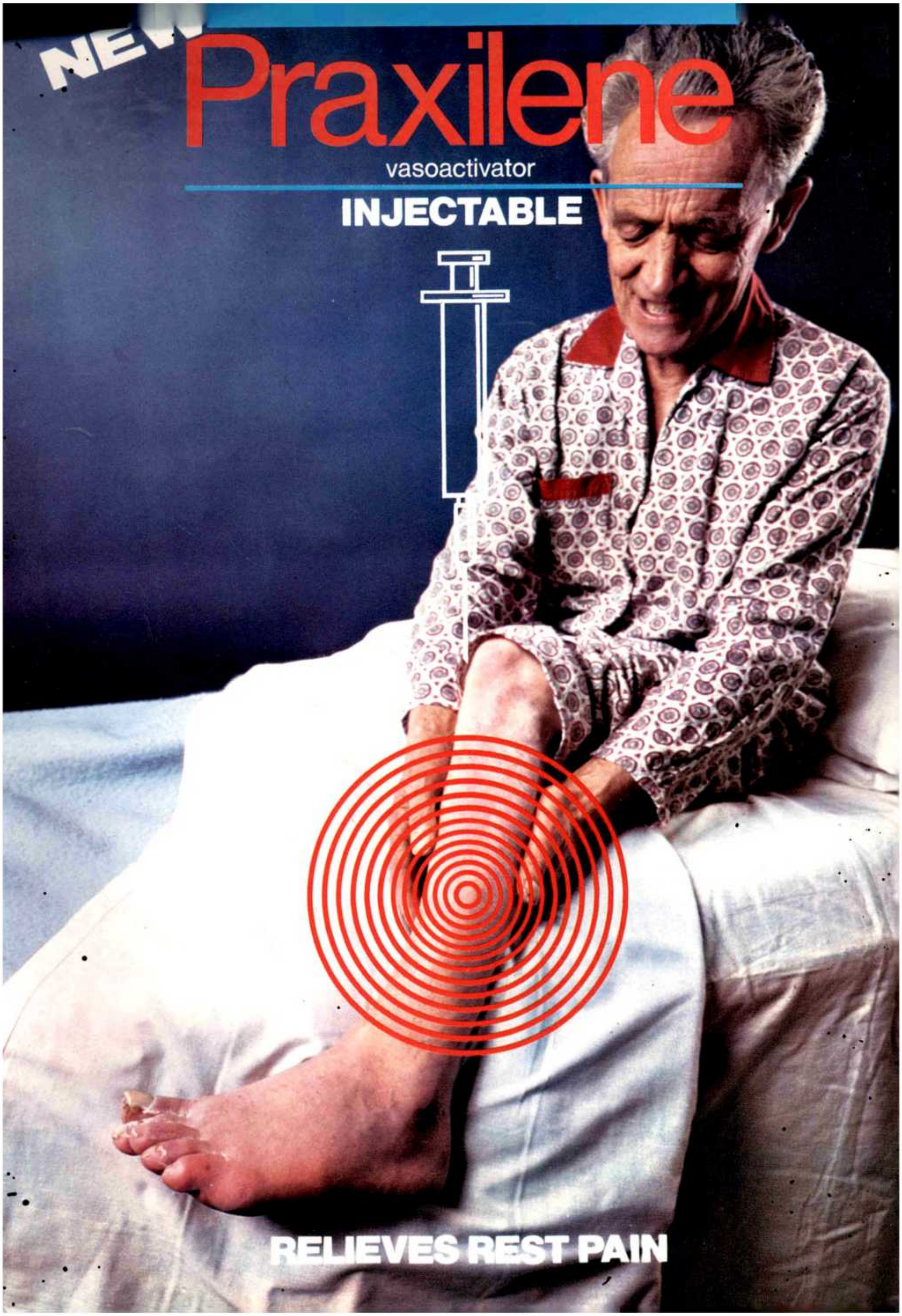
TESLER M. A. and EISENBERG M. M. (1963) Spontaneous esophageal rupture. *Int. Abstr. Surg.* **117**, 1–10.

VOORHEES A. B. jun. (1959) Management of portal hypertension. *Bull. NY Acad. Med.* **35**, 223–230.

WANGENSTEEN S. L., ORAHOOD R. C., VOORHEES A. B., SMITH R. B. and HEALEY W. V. (1963) Intragastric cooling in the management of haemorrhage from the upper gastro-intestinal tract. *Am. J. Surg.* **105**, 401–412.

WANTZ G. E. jun. (1957) Emergency decompression in the treatment of acute haemorrhage from oesophago-gastric varices. In: ELLISON E. H., FRIESEN S. R. and MULHOLLAND J. H. (ed.) *Current Surgical Management III.* London, Saunders pp. 251–258.

WELCH C. S. (1956) Ligation of esophageal varices by the transabdominal route. *New Engl. J. Med.* **255**, 677–683.


NEW
Praxilene
vasoactivator
INJECTABLE
RELIEVES REST PAIN

NEW

for peripheral vascular disorders

Praxilene

vasoactivator

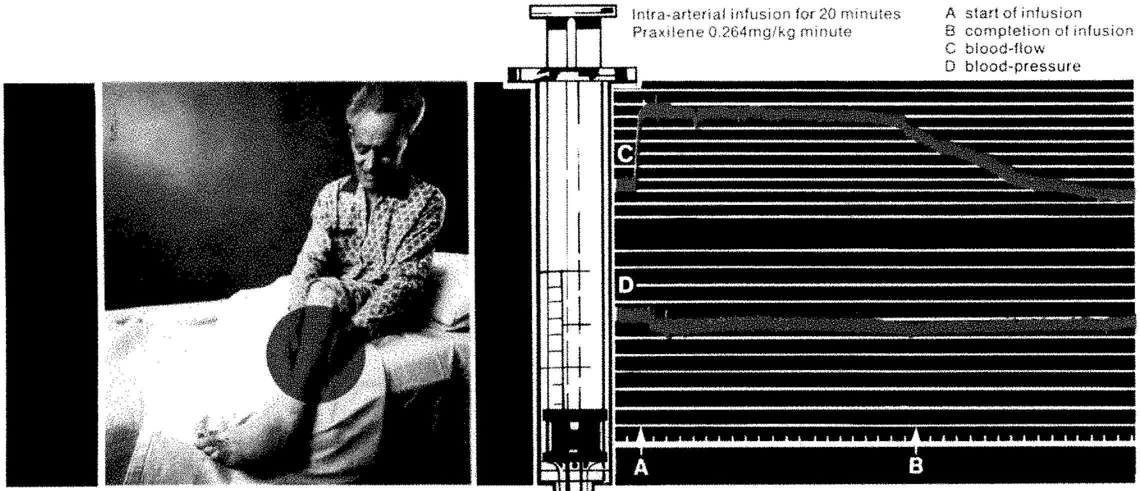
INJECTABLE

RELIEVES REST PAIN

by flushing out pain producing metabolites

by improving blood-flow – without affecting blood-pressure

by a unique metabolic activity



Fast relief

Praxilene administered parenterally (Intra-arterial; Intravenous; Intramuscular) can give relief of pain within as short a time as one week, in many cases.

Prolonged relief

Relief of pain is prolonged: at the same time the collateral circulation is given the opportunity to develop, resulting in an improved blood supply to the affected limb.

Praxilene has produced excellent results because it has a very wide safety margin and the dosage can be individually tailored to the severity of the disorder.

Praxilene: Unique Vasoactivator

Praxilene: Naftidrofuryl: available as 40mg ampoules and 100mg capsules.

Full prescribing information and dosage schedule on request

Lipha (UK)

West Drayton, Middlesex

Telephone: West Drayton 49331/2

Br. J. Surg. Vol. 62 (1975) 113–114

Decreased incidence of indomethacin-induced gastric ulceration in rats by bile duct diversion

FOROOGH S. ABTAHI AND BIJAN DJAHANGUIRI*

SUMMARY

Gastric mucosal ulceration was produced in rats following intraperitoneal injection of indomethacin (40 mg/kg). The incidence of ulcerations was progressively reduced as the bile flow was diverted progressively distal to the ampulla of Vater. It is suggested that bile reflux into the stomach may play a part in the pathogenesis of indomethacin-induced gastric ulceration in rats.

INDOMETHACIN has been known to produce gastric mucosal ulceration in man (Norcross, 1963) and laboratory animals (Menguy and Desbaillets, 1967; Djahanguiri, 1969). The mechanism of the ulcerogenic action of this substance is not well understood. According to Menguy and Desbaillets (1967) indomethacin administration in the dog decreased the rate of mucous secretion and lowered the concentration of carbohydrate, particularly sialic acid and L-fucose, in the mucosubstance. Nicoloff (1968) demonstrated that gastric juice output from vagally denervated fundic pouches is decreased and parietal cell population and mucosal thickness are essentially unchanged after indomethacin administration. A selective increase in gastric blood flow was also noted in dogs ingesting the drug (Edlich et al., 1970). Kent et al. (1969) showed that pretreatment of animals with neomycin, polymycin B and bacitracin reduced the severity of indomethacin-induced ulceration in the stomach, jejunum and ileum. They concluded that the intestinal flora plays a role in the development of ulcers.

We have previously demonstrated that indomethacin-induced gastric ulceration in the rat is prevented by bile duct or pylorus ligation (Hemmati et al., 1974). The same results have been obtained in rats treated with aspirin (Djahanguiri et al., 1973). Therefore we suggested that bile reflux into the stomach may play a part in the pathogenesis of aspirin or indomethacin-induced gastric mucosal lesion.

In the present investigation we have studied the effect of bile drainage into different sites of the small bowel on the incidence of gastric ulceration produced by indomethacin in rats.

Materials and methods

Sprague-Dawley rats of both sexes weighing 180–250 g were used. They were fasted for 24 hours before the experiment, but had free access to water. The animals were divided into seven groups of 20 rats each. The animals in the first group were left untouched. The remaining animals were anaesthetized with ether and their abdomen opened. The second group was considered as sham operated and the abdomens of the animals in this group were closed. In groups 3, 4, 5, 6 and 7 a polyethylene cannula was inserted into the bile duct so that the pancreatic juice flow was not impaired. The other end of the cannula was inserted into the small bowel 0, 2·5, 5, 7·5 and 10 cm respectively distal to the ampulla of Vater. Both ends of the cannula were tied off gently, providing free passage of both bile and small bowel contents. The animals in each group were divided into two subgroups of 10 rats, providing control and experimental groups. Ten minutes after the animals recovered from anaesthesia they received either saline or indomethacin. The control animals received 1 ml/200 g body weight of 0·85 per cent saline solution. Indomethacin was suspended in 0·85 per cent saline solution and administered to the experimental rats at a dose of 40 mg/kg in a volume of 1 ml/200 g body weight. Injections were made by the intraperitoneal route. Four hours after saline or indomethacin administration the animals were sacrificed by a blow on the head. The stomachs were opened and inspected for the presence of ulceration by an observer who was not aware of the experimental protocol, in order to exclude bias. Although a number of investigators have used different criteria as evidence of ulceration, we considered macroscopically necrohaemorrhagic spots larger than 2 mm in diameter as evidence of ulceration. The frequency of these spots, found in the glandular part of the stomach, ranged from 2 to 15. Microscopic examination of ulcer-containing stomachs, chosen at random, confirmed the presence of ulceration in the mucosal layer, rarely reaching the muscularis mucosa, and always accompanied by oedema, necrosis, haemorrhage and infiltration of inflammatory cells. The macroscopic and microscopic findings in both techniques, in positive cases, were the same; χ^2 test was used for the statistical analysis of the data (Armitage, 1971).

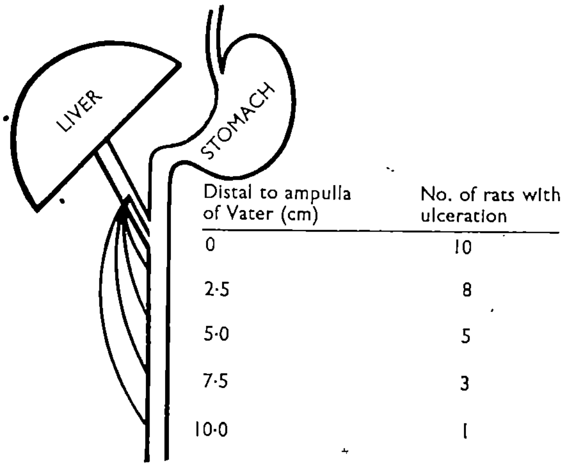
Results

None of the control animals had a gastric mucosal lesion. Indomethacin produced ulceration in 100 per cent of the unoperated and sham-operated animals. The percentages of rats with ulceration in the operated animals were 100, 80, 50, 30 and 10 per cent in

---

* Department of Pharmacology, Faculty of Medicine, University of Tehran, Iran.

Correspondence and reprints to B. Djahanguiri.



Distal to ampulla of Vater (cm)	No. of rats with ulceration
0	10
2·5	8
5·0	5
7·5	3
10·0	1

Fig. 1. Number of rats with gastric ulceration 4 hours following bile duct diversion and indomethacin administration. Ten rats were used in each group.

groups 3, 4, 5, 6 and 7 respectively (*Fig.* 1). The incidence of indomethacin-induced ulceration is significantly ($P < 0{\cdot}001$) reduced in groups 5, 6 and 7 compared with groups 1, 2 and 3. The results show that the incidence of ulceration was progressively reduced as the bile flow was diverted progressively distal to the ampulla of Vater.

Discussion

The results of the present experiment show that exclusion of bile reflux from the stomach prevents the appearance of indomethacin-induced gastric ulceration in rats fasted for 24 hours. Although this experimental model of drug-induced gastric ulceration has not been proved to be similar to human acute gastritis, the operation performed in this experiment is similar to that reported by Scudamore et al. (1973), who successfully treated 13 patients with bile reflux gastritis with a Roux-en-Y type of operation to prevent bile reflux. They anastomosed the biliary branch of the Y to the jejunum 50–60 cm distal to the gastrojejunal anastomosis. We have previously observed that bile duct or pylorus ligation prevents indomethacin-induced as well as aspirin-induced gastric lesions in rats. Moreover, Capper et al. (1966) have injected barium into the duodenum and have studied duodenal reflux radiologically. Nineteen out of 29 patients with gastric ulcer had duodenal reflux compared with none of the 15 control subjects.

From these findings it is suggested that bile reflux plays a part in the pathogenesis of indomethacin-induced gastric ulceration in rats. The effect of bile in the stomach is not known. Bile salts have been shown to be cytolytic, to damage the gastric mucosa and to release gastrin (Nahrwold, 1972). However, the precise mechanism whereby the presence of bile in the stomach promotes the pathogenesis of gastric ulceration following indomethacin administration is not clear.

Acknowledgement

The generous supply of indomethacin (Indocid) by Merck, Sharp & Dohme Pharmaceutical Co. is gratefully acknowledged.

References

ARMITAGE P. (1971) *Statistical Methods in Medical Research*. New York, Wiley, pp. 131–134.

CAPPER W. M., AIRTH G. R. and KILBY J. O. (1966) A test for pyloric regurgitation. *Lancet* **2**, 621–623.

DJAHANGUIRI B. (1969) The production of acute gastric ulceration by indomethacin in the rat. *Scand. J. Gastroenterol.* **4**, 265–267.

DJAHANGUIRI B., ABTAHI F. and HEMMATI M. (1973) Prevention of aspirin-induced gastric ulceration by bile duct or pylorus ligation in the rat. *Gastroenterology* **65**, 630–633.

EDLICH R. F., NICOLOFF D. M., BORGEN L., BUCHIN R. and WANGENSTEEN O. W. (1970) Gastric blood flow and its distribution during indomethacin administration. *Surg. Gynecol. Obstet.* **130**, 789–793.

HEMMATI M., ABTAHI F., FARROKHSIAR M. and DJAHANGUIRI B. (1974) Prevention of restraint and indomethacin-induced gastric ulceration by bile duct or pylorus ligation in rats. *Digestion* **10**, 108–112.

KENT T. H., CARDELLI R. M. and STAMLER F. W. (1969) Small intestinal ulcers and intestinal flora in rats given indomethacin. *Am. J. Pathol.* **54**, 237–245.

MENGUY R. and DESBAILLETS L. (1967) Role of inhibition of acid mucous secretion in the phenomenon of gastric mucosal injury by indomethacin. *Am. J. Dig. Dis.* **12**, 862–866.

NAHRWOLD D. L. (1972) Bile as a gastric secretory stimulant. *Surgery* **71**, 157–160.

NICOLOFF D. M. (1968) Indomethacin: effect on gastric secretion, parietal cell population and ulcer provocation in the dog. *Arch. Surg.* **97**, 809–815.

NORCROSS B. M. (1963) Treatment of connective tissue disease with a new nonsteroidal compound (indomethacin). *Arthritis Rheum.* **6**, 290–295.

SCUDAMORE H. H., EKSMAN E. E., FENCIL W. J. and JARAMILLO C. A. (1973) Bile reflux gastritis. *Am. J. Gastroenterol.* **60**, 9–22.

Br. J. Surg. Vol. 62 (1975) 115–118

The aetiology of hypocalcaemia in acute pancreatitis

JOHN R. CONDON, DAVID IVES, MICHAEL J. KNIGHT AND JOHN DAY*

SUMMARY

Plasma calcitonin, glucagon and parathyroid hormone were measured in patients with acute pancreatitis.

Plasma calcitonin was not detectable in 6 specimens obtained from the hypocalcaemic patients.

Plasma glucagon values were similar in patients with acute pancreatitis and control subjects and were unrelated to hypocalcaemia, which was not even induced by glucagon infusion.

High or rising parathyroid hormone levels were noted in association with hypo- and normocalcaemia, suggesting that parathyroid hormone rises and maintains plasma calcium within normal limits. Plasma parathyroid hormone was, however, undetectable in 8 patients with prolonged hypocalcaemia. Deficiency of parathyroid hormone due to its destruction by proteolytic enzymes or because of parathyroid gland exhaustion is suggested as the major factor inducing persistent hypocalcaemia in acute pancreatitis. Administration of parathyroid hormone should, therefore, be considered in patients with acute pancreatitis when hypocalcaemia does not respond to intravenous calcium therapy.

HYPOCALCAEMIA occurring in patients with acute pancreatitis was originally thought to be due to the deposition of calcium in areas of fat necrosis (Langerhans, 1890; Edmondson and Fields, 1942). More recently, Paloyan, Lawrence et al. (1966) suggested that hyperglucagonaemia occurred in acute pancreatitis; this might induce hypocalcaemia either by releasing calcitonin (Pickleman et al, 1969; Shieber et al., 1969) or by directly inhibiting bone resorption (Stern and Bell, 1970; Tanzer et al., 1970). A third possible cause of hypocalcaemia in acute pancreatitis is failure of parathyroid hormone to mobilize calcium from bone (Hernandez et al., 1961). This could be due to defective secretion of the hormone by the parathyroid glands, chemical degradation and inactivation of the hormone by proteolytic enzymes in the peripheral circulation or lastly inhibition of parathyroid hormone-stimulated bone resorption by glucagon and/or calcitonin (Raisz et al., 1968; Condon, 1971).

We have investigated these possible mechanisms by measuring circulating parathyroid hormone, glucagon, calcitonin and calcium in patients with acute pancreatitis. The effect of glucagon on calcium metabolism was also studied in patients with acute pancreatitis treated with the hormone (Knight et al., 1971; Condon et al., 1973).

Materials and methods

Plasma calcium was determined by atomic absorption spectrophotometry.

Parathyroid hormone was measured by radioimmunoassay. The antisera used was raised in guinea-pigs against bovine parathyroid hormone (B W 211/32); an uncoated charcoal technique was used.

Glucagon was measured by radio-immunoassay using spherocil-extracted samples and a specific antiserum for pancreatic glucagon (Day et al., 1972).

Calcitonin was determined by Dr G. V. Foster by radio-immunoassay (Clark et al., 1969).

Thirty patients with acute pancreatitis were investigated. The diagnosis was confirmed at operation in 13 cases, while the other 17 patients had abdominal pain and a high plasma amylase (>1000 Somogyi units/100 ml).

Hypocalcaemia (plasma calcium <8·9 mg/100 ml) was observed in 12 cases. Parathyroid hormone was assayed on 21 samples in 11 hypocalcaemic patients and on 13 samples in 3 normocalcaemic subjects. Plasma glucagon was measured in all these subjects. Plasma calcitonin was assayed on 6 samples in 2 of these hypocalcaemic cases and another hypocalcaemic patient. Plasma glucagon was also measured in 12 other normocalcaemic patients with pancreatitis. In 11 of these subjects plasma calcium and glucagon were measured before and 1 and 12 hours after giving glucagon (an initial bolus dose of 1 mg intravenously followed by a continuous intravenous infusion at 1–1½ mg 4-hourly).

Results

Parathyroid hormone was undetectable in the plasma of 8 patients with hypocalcaemia (calcium: range 6·7–8·8, mean 7·8 mg/100 ml). One patient with a plasma calcium of 8·5 mg/100 ml had an elevated parathyroid hormone level of 675 pg/ml, while 3 other subjects had plasma parathyroid hormone levels of 100–175 pg/ml. One of these subjects was hypocalcaemic (plasma calcium 8·5 mg/100 ml), while 2 were normocalcaemic (plasma calcium 9·0–9·9 mg/100 ml).

Serial changes in plasma parathyroid hormone were noted in 3 subjects. The first had a markedly elevated level of 1·5 ng/ml when the plasma calcium was 8·9 mg/100 ml. A second sample 24 hours later showed a marked fall in parathyroid hormone to 0·5 ng/ml and a fall in plasma calcium to 8·5 mg/100 ml. The second subject (*Fig.* 1) initially had a high plasma parathyroid hormone level and was normocalcaemic; plasma parathyroid hormone fell gradually but the

---

* J. R. Condon: St Mary's Hospital, Eastbourne.
D. Ives: Metabolic Unit, University College Hospital, London.
M. J. Knight: St George's Hospital, London.
J. Day: Ipswich Group of Hospitals.

Br. J. Surg. Vol. 62 (1975) 115–118

The aetiology of hypocalcaemia in acute pancreatitis

JOHN R. CONDON, DAVID IVES, MICHAEL J. KNIGHT AND JOHN DAY*

SUMMARY

Plasma calcitonin, glucagon and parathyroid hormone were measured in patients with acute pancreatitis.

Plasma calcitonin was not detectable in 6 specimens obtained from the hypocalcaemic patients.

Plasma glucagon values were similar in patients with acute pancreatitis and control subjects and were unrelated to hypocalcaemia, which was not even induced by glucagon infusion.

High or rising parathyroid hormone levels were noted in association with hypo- and normocalcaemia, suggesting that parathyroid hormone rises and maintains plasma calcium within normal limits. Plasma parathyroid hormone was, however, undetectable in 8 patients with prolonged hypocalcaemia. Deficiency of parathyroid hormone due to its destruction by proteolytic enzymes or because of parathyroid gland exhaustion is suggested as the major factor inducing persistent hypocalcaemia in acute pancreatitis. Administration of parathyroid hormone should, therefore, be considered in patients with acute pancreatitis when hypocalcaemia does not respond to intravenous calcium therapy.

HYPOCALCAEMIA occurring in patients with acute pancreatitis was originally thought to be due to the deposition of calcium in areas of fat necrosis (Langerhans, 1890; Edmondson and Fields, 1942). More recently, Paloyan, Lawrence et al. (1966) suggested that hyperglucagonaemia occurred in acute pancreatitis; this might induce hypocalcaemia either by releasing calcitonin (Pickleman et al, 1969; Shieber et al., 1969) or by directly inhibiting bone resorption (Stern and Bell, 1970; Tanzer et al., 1970). A third possible cause of hypocalcaemia in acute pancreatitis is failure of parathyroid hormone to mobilize calcium from bone (Hernandez et al., 1961). This could be due to defective secretion of the hormone by the parathyroid glands, chemical degradation and inactivation of the hormone by proteolytic enzymes in the peripheral circulation or lastly inhibition of parathyroid hormone-stimulated bone resorption by glucagon and/or calcitonin (Raisz et al., 1968; Condon, 1971).

We have investigated these possible mechanisms by measuring circulating parathyroid hormone, glucagon, calcitonin and calcium in patients with acute pancreatitis. The effect of glucagon on calcium metabolism was also studied in patients with acute pancreatitis treated with the hormone (Knight et al., 1971; Condon et al., 1973).

Materials and methods

Plasma calcium was determined by atomic absorption spectrophotometry.

Parathyroid hormone was measured by radio-immunoassay. The antisera used was raised in guinea-pigs against bovine parathyroid hormone (B W 211/32); an uncoated charcoal technique was used.

Glucagon was measured by radio-immunoassay using spherocil-extracted samples and a specific antiserum for pancreatic glucagon (Day et al., 1972).

Calcitonin was determined by Dr G. V. Foster by radio-immunoassay (Clark et al., 1969).

Thirty patients with acute pancreatitis were investigated. The diagnosis was confirmed at operation in 13 cases, while the other 17 patients had abdominal pain and a high plasma amylase (>1000 Somogyi units/100 ml).

Hypocalcaemia (plasma calcium <8·9 mg/100 ml) was observed in 12 cases. Parathyroid hormone was assayed on 21 samples in 11 hypocalcaemic patients and on 13 samples in 3 normocalcaemic subjects. Plasma glucagon was measured in all these subjects. Plasma calcitonin was assayed on 6 samples in 2 of these hypocalcaemic cases and another hypocalcaemic patient. Plasma glucagon was also measured in 12 other normocalcaemic patients with pancreatitis. In 11 of these subjects plasma calcium and glucagon were measured before and 1 and 12 hours after giving glucagon (an initial bolus dose of 1 mg intravenously followed by a continuous intravenous infusion at 1–1½ mg 4-hourly).

Results

Parathyroid hormone was undetectable in the plasma of 8 patients with hypocalcaemia (calcium: range 6·7–8·8, mean 7·8 mg/100 ml). One patient with a plasma calcium of 8·5 mg/100 ml had an elevated parathyroid hormone level of 675 pg/ml, while 3 other subjects had plasma parathyroid hormone levels of 100–175 pg/ml. One of these subjects was hypocalcaemic (plasma calcium 8·5 mg/100 ml), while 2 were normocalcaemic (plasma calcium 9·0–9·9 mg/100 ml).

Serial changes in plasma parathyroid hormone were noted in 3 subjects. The first had a markedly elevated level of 1·5 ng/ml when the plasma calcium was 8·9 mg/100 ml. A second sample 24 hours later showed a marked fall in parathyroid hormone to 0·5 ng/ml and a fall in plasma calcium to 8·5 mg/100 ml. The second subject (*Fig.* 1) initially had a high plasma parathyroid hormone level and was normocalcaemic; plasma parathyroid hormone fell gradually but the

---

* J. R. Condon: St Mary's Hospital, Eastbourne.
D. Ives: Metabolic Unit, University College Hospital, London.
M. J. Knight: St George's Hospital, London.
J. Day: Ipswich Group of Hospitals.

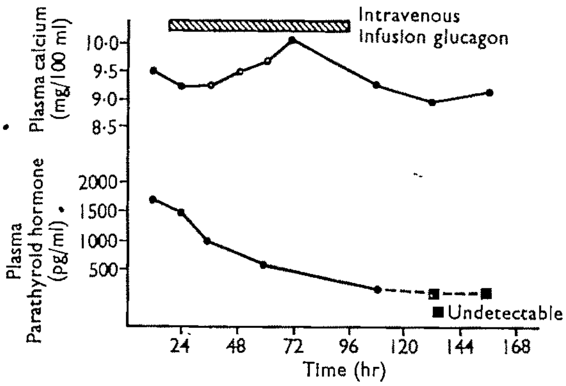


Fig. 1. Serial changes in plasma parathyroid hormone in a normocalcaemic subject.

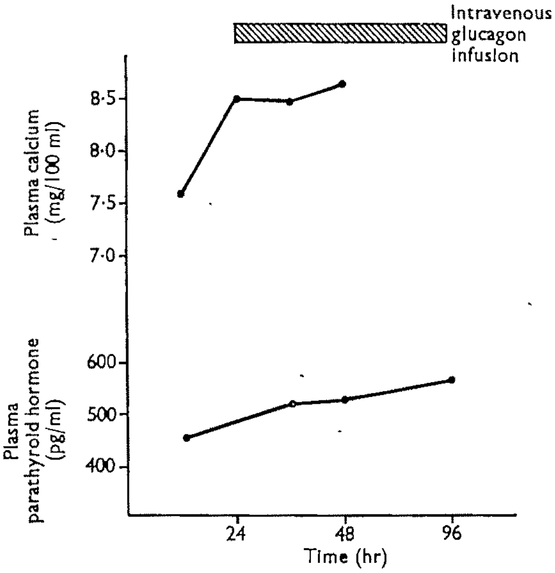


Fig. 2. Serial changes in plasma parathyroid hormone in a patient who was initially hypocalcaemic.

plasma calcium remained within normal limits. Glucagon infused intravenously did not result in hypocalcaemia. The third patient (*Fig.* 2) was initially hypocalcaemic, but later plasma parathyroid hormone and plasma calcium both rose; glucagon infusion was not associated with hypocalcaemia.

Calcitonin was undetectable in 6 plasma samples assayed in 3 hypocalcaemic patients (assay limit of detection, 500 pg/ml).

The mean fasting plasma glucagon level in 15 normal subjects was 0·48 (±0·08) ng/ml, and in 26 patients with acute pancreatitis 0·45 (±0·07) ng/ml. Following glucagon infusion, mean plasma glucagon rose significantly ($P < 0{\cdot}025$) at 1 hour by 3·4 to 4 ng/ml, except in 2 patients whose plasma glucagon rose from 0·25 to 0·33 ng/ml and fell from 0·63 to 0·54 ng/ml respectively. These 2 subjects showed a significant increase in plasma glucagon to 0·68 and 2·2 ng/ml respectively 12 hours after starting the glucagon infusion. There was no significant difference between plasma glucagon values at 1 and 12 hours following glucagon infusion. Plasma calcium showed no significant fall from 0 to 1 hour but fell significantly from 0 to 12 hours ($P < 0{\cdot}025$); the difference between plasma calcium at 1 and 12 hours was also significant ($P < 0{\cdot}025$). However, the correlation between the change in plasma glucagon with change in plasma calcium between 0 and 1 hour showed that the greater the increase in glucagon concentration the smaller was the fall in plasma calcium. At 12 hours there was no significant relationship between the fall in plasma calcium with change in plasma glucagon concentration either from the pre-infusion value or from the 1-hour value after the onset of glucagon infusion.

Discussion

Our findings indicate that persistent hypocalcaemia associated with acute pancreatitis is due to relative deficiency of parathyroid hormone and is unrelated to plasma glucagon and calcitonin levels. These conclusions are based on the fact that no parathyroid hormone was detectable in the plasma of 8 patients with hypocalcaemic acute pancreatitis. Furthermore, in 1 patient plasma parathyroid hormone fell from 1·5 to 0·5 ng/ml despite a fall in plasma calcium from 8·9 to 8·5 mg/100 ml, although one would have reasonably expected plasma parathyroid hormone to have risen in the presence of hypocalcaemia. On the other hand, plasma parathyroid hormone was detectable in a number of patients with normocalcaemic pancreatitis, indicating maintenance of normal plasma calcium levels by the action of parathyroid hormone on bone and kidney.

There is no doubt that serum levels of parathyroid hormone rise in patients with acute pancreatitis and this is well demonstrated in *Fig.* 1, which shows high levels of parathyroid hormone in a normocalcaemic patient. Normally, plasma parathyroid hormone levels rise in response to an acute fall in plasma calcium (Ramberg et al., 1967; Buckle, 1970), so that the patient whose hormone levels are represented in *Fig.* 1 must have had an initial fall in plasma calcium which triggered off increased secretion of parathyroid hormone. The resultant correction of plasma calcium by the actions of parathyroid hormone reduces further secretion of the hormone by the calcium feedback mechanism, blood levels of parathyroid hormone gradually falling to undetectable concentrations as demonstrated in our patient. The concept of an increasing parathyroid hormone concentration in response to hypocalcaemia in acute pancreatitis is supported by the findings in another patient (*Fig.* 2) in whom plasma parathyroid hormone levels gradually rose in association with a rising plasma calcium. Thus, although it is clear that plasma parathyroid hormone levels may rise in acute pancreatitis and correct any initial fall in plasma calcium, we have also shown that an elevated plasma concentration of parathyroid hormone is not a characteristic feature of patients with persistent hypocalcaemic acute pancreatitis, strongly suggesting the presence of a relative deficiency of parathyroid hormone in these patients.

Further evidence in support of the concept that persistent hypocalcaemia in acute pancreatitis is due to a deficiency of parathyroid hormone is provided by the findings of Hayes (1955) and Hernandez et al. (1961), who showed that intravenously administered parathyroid hormone corrected hypocalcaemia in patients with acute pancreatitis who had previously not responded to intravenous calcium therapy.

One possible explanation to account for the apparent parathyroid hormone deficiency in patients with acute hypocalcaemic pancreatitis is failure of the parathyroid glands to maintain secretion of the hormone. It is generally believed that the parathyroid glands store only small quantities of parathyroid hormone and it is possible that they become rapidly depleted of hormone in the presence of continued hypocalcaemic stress. Alternatively, there may be increased inactivation of circulating parathyroid hormone by proteolytic enzymes, and in support of this possibility is the fact that proteolysis of plasma proteins is known to occur following incubation with trypsin (Rocha e Silva et al., 1949).

We have also attempted to elucidate the role of the hormones glucagon and calcitonin in the pathogenesis of hypocalcaemia in acute pancreatitis. Elevated plasma glucagon has been reported in patients with pancreatitis and in dogs with experimental pancreatitis (Paloyan, Lawrence et al., 1966; Paloyan, Paloyan et al. 1966). Since glucagon induces a fall in plasma calcium it was suggested that hyperglucagonaemia might contribute to hypocalcaemia associated with acute pancreatitis (Paloyan et al., 1967; Cortes, 1971). A raised plasma glucagon might induce hypocalcaemia by direct action on bone (Stern and Bell, 1970) or by release of calcitonin from the thyroid gland (Care et al., 1970).

In dogs with experimental pancreatitis plasma glucagon levels first rise and later fall before the death of the animal (Knight et al., 1972). In patients with acute haemorrhagic pancreatitis plasma glucagon levels are low (Day et al., 1972), whereas in non-haemorrhagic acute pancreatitis plasma glucagon levels are not significantly different from those of normal fasting subjects. In all these experimental and clinical studies there is no correlation between changes in plasma calcium and glucagon levels. Furthermore, during intravenous infusion of glucagon in 11 of our patients there was no quantitative relationship between plasma calcium and glucagon concentrations despite marked rises in plasma levels of glucagon. Indeed, much larger doses of glucagon produce only mild hypocalcaemia in man, 2 mg given intravenously over a 5-minute period resulting in a fall in plasma calcium of 0·05 to 1 mg/100 ml (Condon, 1973).

We have studied one other possible contributory factor, namely calcitonin, a hormone which is released from the thyroid glands of animals by glucagon (Care et al., 1970).

No calcitonin was detectable by radio-immunoassay in the plasma of 3 patients with marked hypocalcaemia associated with pancreatitis. This does not exclude the possibility of elevated plasma calcitonin levels below the limit of detection of the assay (500 pg/ml). Elevated calcitonin levels are, however, unlikely to result in severe hypocalcaemia since a low plasma calcium is not a feature of patients with medullary cell carcinoma of the thyroid who have high plasma hormone levels (Cunliffe et al., 1968; Tubiana et al., 1968; Milhaud et al., 1969).

There has in the past been no general agreement as to the factors accounting for a fall in plasma calcium in acute pancreatitis. The calcium soap theory appears an inadequate explanation since serum calcium often remains unchanged despite administration of intravenous calcium in doses equal to or greater than the amount of calcium calculated to be bound to the necrotic fatty tissue of patients with acute hypocalcaemic pancreatitis. Even if plasma glucagon and calcitonin concentrations were to increase for a short period of time during the development of acute pancreatitis only a small fall in plasma calcium is to be expected, since in the presence of normal parathyroid gland function serum calcium is rapidly restored to normal. We, therefore, propose that there is an immediate fall in plasma calcium in acute pancreatitis due to precipitation of calcium in areas of fat necrosis and less probably an elevation of both plasma glucagon and calcitonin concentration for a short period of time. Plasma calcium is rapidly restored to normal by increased secretion of parathyroid hormone, but in patients with persistent hypocalcaemic pancreatitis, plasma parathyroid hormone fails to rise because of either decreased secretion or increased proteolytic degradation of the hormone. If this interpretation of our findings is correct parathyroid hormone may be of therapeutic use in patients with acute pancreatitis who have persistent hypocalcaemia which is resistant to calcium therapy; likewise the vitamin D metabolite 25-hydroxy-colecalciferol may also be of benefit in this condition.

References

BUCKLE R. M. (1970) The relation of serum parathyroid hormone to serum calcium and magnesium levels. *Proc. R. Soc. Med.* **63**, 871–875.

CARE A. D., BATES R. F. L. and GITELMAN J. H. (1970) A possible role for the adenyl cyclase system in calcitonin release. *J. Endocrinol.* **41**, 1–15.

CLARK M. B., BOYD G. W., BYFIELD P. G. H. and FOSTER G. W. (1969) A radio-immunoassay for human calcitonin M. *Lancet* **2**, 74–77.

CONDON J. R. (1971) Glucagon in the treatment of Paget's disease of bone. *Br. Med. J.* **4**, 719–721.

CONDON J. R. (1973) Personal observation.

CONDON J. R., KNIGHT M. J., DAY J. (1973) Glucagon therapy in acute pancreatitis. *Br. J. Surg.* **60**, 509–511.

CORTES E. P. (1971) Pancreatitis and serum calcium. *Ann. Intern. Med.* **74**, 1014.

CUNLIFFE W. J., BLACK M. M., HALL R., JOHNSTON I. D. A., HUDGSON P., SHUSTER S., GUDMUNDSON T. U., JOPLIN G. F., WILLIAMS E. D., WOODHOUSE N. J. Y., GALANT L. and MACINTYRE I. (1968) A calcitonin-secreting thyroid carcinoma. *Lancet* **2**, 63–66.

DAY J., KNIGHT M. J. and CONDON J. R. (1972) The role of pancreatitis glucagon in the pathogenesis of acute pancreatitis. *Clin. Sci.* **43**, 597–603.

EDMONDSON H. A. and FIELDS I. (1942) Relation of calcium and lipids to acute pancreatic necrosis. *Arch. Intern. Med.* **69**, 177–190.

HAYES M. A. (1955) A disturbance in calcium metabolism leading to tetany occurring early in acute pancreatitis. *Ann. Surg.* **142**, 346–350.

HERNANDEZ I. A., POWERS S. R. and FRAWLEY T. F. (1961) The role of parathyroid glands in calcium and magnesium metabolism in acute haemorrhagic pancreatitis. *Surgery* **50**, 143–150.

KNIGHT M. J., CONDON J. R. and DAY J. (1972) Possible role of glucagon in pathogenesis of acute pancreatitis. *Lancet* **1**, 1097–1099.

KNIGHT M. J., CONDON J. R. and SMITH R. (1971) Possible use of glucagon in the treatment of pancreatitis. *Br. Med. J.* **2**, 440–442.

LANGERHANS R. (1890) Ueber multiple Fettgewebsnekrose. *Virchows Arch. Pathol. Anat.* **122**, 252–270.

MILHAUD G., COUTRIS G. and TUBIANA M. (1969) Le cancer médullaire de la thyroïde et le syndrome d'hyperthyrocalcitonin. *Presse Méd.* **77**, 2129–2132.

PALOYAN E., LAWRENCE A., ERNST K., WOROBEC R., DEININGER E., PALOYAN D. and HARPER P. V. (1966) *Fed. Proc.* Abstract 1717, **25**(i), 495.

PALOYAN D., PALOYAN E. and HARPER P. V. (1967) Glucagon-induced hypocalcaemia. *Metabolism* **16**, 35–39.

PALOYAN D., PALOYAN E., WOROBEC R., ERNST K., DEININGER E. and HARPER P. V. (1966) Serum glucagon levels in experimental acute pancreatitis in the dog. *Surg. Forum* **17**, 348–349.

PICKLEMAN J. R., ERNST K., BROWN S. and PALOYAN E. (1969) Glucagon induced hypocalcaemia: effect of the thyroid gland. *Surg. Forum* **20**, 85–87.

RAISZ L. G., AU W. Y. W., FRIEDMAN J. and NIEMANN I. (1968) Inhibition of bone resorption in tissue culture by thyrocalcitonin. In: TAYLOR S. (ed.) *Proceedings of Symposium on Thyrocalcitonin and the C Cells.* London, Heinemann, pp. 215–222.

RAMBERG C. F., MAYER G. P., KRONFELD D. S., AURBACH G. D., SHERWOOD L. M. and POTTS J. T. (1967) Plasma calcium and parathyroid hormone response to EDTA infusion in the cow. *J. Physiol.* **213**, 878–882.

ROCHA E SILVA M., BERALDO W. T. and ROSENFELD G. (1949) Bradykinin, a hypotensive and smooth muscle stimulating factor released from plasma globulin by snake venom and by trypsin. *Am. J. Physiol.* **156**, 261–273.

SHIEBER W., AVIOLI L. V., BIRGE S. J. and SCOTT S. (1969) Mechanism of action of glucagon-induced hypocalcaemia. *Surg. Forum* **20**, 87–89.

STERN P. H. and BELL N. H. (1970) Effect of glucagon on serum calcium in the rat and on bone resorption in tissue culture. *Endocrinology* **87**, 111–117.

TANZER F. S., KENNEDY J. W. and TALMAGE R. V. (1970) A comparison of the effect of thyrocalcitonin and glucagon on plasma calcium and phosphate. *Proc. Soc. Exp. Biol. Med.* **133**, 500–505.

TUBIANA M., MILHAUD G., COUTRIS G., LACOUR J., PARMENTIER C. and BOK B. (1968) Medullary carcinoma and thyrocalcitonin. *Br. Med. J.* **4**, 87–89.

Br. J. Surg. Vol. 62 (1975) 119–120

An appraisal of peritoneal lavage in the diagnosis of the acute abdomen

CHRISTINE EVANS, A. RASHID, I. L. ROSENBERG
AND A. V. POLLOCK*

SUMMARY

Forty-seven selected patients presenting with acute abdominal symptoms were investigated by examination of the fluid obtained by peritoneal lavage. In 34 patients this confirmed the clinical diagnosis, in 11 it was a more positive help in that it corrected an erroneous clinical diagnosis and in 2 the results of the investigation were misleading.

In the diagnosis of acute abdominal emergencies the experienced clinician achieves an accuracy of almost 80 per cent. With the help of a computer programed to accept important aspects of history and physical signs, this approaches 92 per cent (de Dombal et al., 1972). There are certain situations, however, in which it is difficult to make a confident diagnosis. These often arise because of poor cooperation from the patient due to age, low intelligence, altered consciousness or the presence of severe injuries elsewhere. It is for these patients that examination of the peritoneal fluid can be a valuable adjunct to familiar radiological and laboratory investigations. We favour peritoneal lavage, as it is often impossible to obtain fluid by mere paracentesis.

Materials and methods

Peritoneal lavage was not a routine examination for all patients with acute abdominal symptoms, but 47 were selected for lavage in whom a confident diagnosis could not be made after routine investigations. Abdominal puncture has been avoided in patients with considerable bowel distension or multiple scars which could indicate widespread adhesions.

The patient was usually tranquillized by an intravenous injection of diazepam 10 mg, and the abdominal wall infiltrated with 2 per cent lignocaine. A Dialaflex Mark II dialysis catheter (Allen & Hanburys Ltd, London) was introduced into the peritoneal cavity (usually in the midline below the umbilicus, but avoiding any previous laparotomy scar) and 1 litre of saline or other sterile fluid was run in within 5–10 minutes. The fluid was allowed to remain for 10 minutes, and the patient encouraged to move about if his general condition allowed. The fluid was then drained and after removal of the catheter the skin was closed with a single suture.

We have tried the 'two-needle' modification of the technique published by Civetta et al. (1970), but found it less reliable than the method described here.

Aliquots were taken into sterile containers for bacteriological and biochemical investigations. The most important tests were an examination of a Gram-stained centrifuged deposit for cells and organisms and estimation of the amylase content. The fluid was cultured, but the delay entailed made this of relatively little importance.

Normal fluid contained less than 0·1 × 10^{12} red cells/litre, an occasional polymorph and no organisms; it was sterile, with less than 100 Somogyi units of amylase/100 ml.

Results

Forty-seven patients were selected for this investigation on account of diagnostic difficulty (*Table I*). In 34 the tentative clinical diagnosis was confirmed by the results of examination of the peritoneal fluid, and the final diagnosis agreed with both. Estimation of the amylase content of the fluid was unhelpful. The highest level (3600 u./100 ml) was found in a patient with traumatic rupture of the ileum, and 2 of the 7 patients with acute pancreatitis had less than 100 u./100 ml in the peritoneal fluid.

In contrast with these merely confirmatory results, there were 11 patients in whom the provisional diagnosis was shown to be erroneous by peritoneal lavage, which was therefore of great value (*Table II*).

On the other hand, in 2 patients the returned fluid was normal but serious disease was present. In the first an abdominal X-ray subsequently showed a small amount of air under the right dome of the diaphragm, and the presumed small perforation of a duodenal ulcer was treated conservatively with success. In the second, delayed rupture of the spleen necessitated splenectomy 24 hours after lavage had produced normal fluid. These were the only misleading results.

It must be stressed that lavage can only diagnose the presence or absence of intraperitoneal bleeding or inflammation, and not the cause.

In no patient was any untoward reaction detected, nor was bowel perforated by a dialysis catheter, although we accept that this risk exists (Thal and Shires, 1973). On the contrary, many patients volunteered that they felt better as a result of the 'treatment'.

Discussion

Diagnostic abdominal paracentesis was first reported by Salomon (1906), who described catheterization of the peritoneal cavity through a cannula, with

---

* Scarborough Hospital, Scarborough, Yorkshire.

Table I: RESULTS OF LAVAGE FLUID ANALYSIS

Final diagnosis	Total no. of cases	Normal fluid	Excess RBC	Excess WBC	Organisms	Amylase <100 u./100 ml.	Amylase >100 u./100 ml.	Amylase Not estimated
Perforated peptic ulcer	8	1	5	7	1	5	3	0
Perforated appendix	5	0	2	5	2	3	0	2
Perforated gallbladder	2	0	0	2	0	0	1	1
Perforated ileum	2	0	2	2	0	1	1	0
Pancreatitis	7	0	1	7	0	2	4	1
Other septic peritonitis	8	0	4	8	1	4	2	2
Ruptured solid viscus	5	1	4	0	0	4	0	1
Bronchopneumonia	1	1	0	0	0	1	0	0
Pyelitis	2	2	0	0	0	2	0	0
Non-specific abdominal pain	7	7	0	0	0	6	0	1
Total	47	12	18	31	4	28	11	8

Table II: DETAILS OF 11 PATIENTS IN WHOM PERITONEAL LAVAGE CORRECTLY CONTRADICTED THE PROVISIONAL DIAGNOSIS

Provisional diagnosis	Lavage fluid findings	Final diagnosis	Procedure
Acute cholecystitis	Normal	Bronchopneumonia	No laparotomy
Acute appendicitis	Normal	Non-specific abdominal pain	Negative laparotomy
Peritonitis	Normal	Partial intestinal obstruction	Later laparotomy
Peritonitis	Normal	Urinary tract infection	No laparotomy
Acute cholecystitis	Normal	Carcinoma, transverse colon	Subsequent resection
Peritonitis	Normal	Urinary tract infection	No laparotomy
Peritonitis	Normal	Gallstone colic	No laparotomy
Acute cholecystitis	Normal	Cardiac infarct	No laparotomy
Non-specific abdominal pain	Pus cells Amylase 105	Pancreatic abscess	Laparotomy and drainage
Pancreatitis	*Escherichia coli* Pus cells No amylase	Perforated appendix	Laparotomy and appendicectomy
Bile peritonitis after cholecystectomy	Blood	Haemoperitoneum	No laparotomy

aspiration of fluid for microscopic examination. The method did not become popular, possibly because of Salomon's warning of the dangers of actually causing peritonitis.

It has been resuscitated sporadically, but its value is lessened by the frequent failure to obtain fluid. Four-quadrant (Baker et al., 1967) or pelvic (Gjessing et al., 1972) aspiration has been advocated, but in the presence of localized intraperitoneal inflammatory disease (as opposed to general peritonitis) fluid is unobtainable by any method in 90 per cent of cases (Baker et al., 1967; 'a negative paracentesis has no positive significance').

Root et al. (1965) introduced a refinement of diagnostic paracentesis for the investigation of intra-abdominal injuries due to non-penetrating trauma. Through a dialysis catheter they ran in a litre of fluid and then aspirated it. They were, however, more interested in the haemoglobin content of the returned fluid than in the presence of pus cells.

Subsequent publications have extended the indications for diagnostic peritoneal lavage (as opposed to simple paracentesis) (Veith et al., 1967; Thal and Shires, 1973) and it is now recognized as a useful aid in the diagnosis of the presence of intra-abdominal injury or inflammation.

Regrettably the amylase content of the lavage fluid has not helped in the diagnosis of acute pancreatitis. It was normal in 2 out of the 7 cases, and raised in 7 patients with other forms of peritonitis.

References

BAKER W. N. W., MACKIE D. B. and NEWCOMBE J. F. (1967) Diagnostic paracentesis in the acute abdomen. *Br. Med. J.* **3**, 146–149.

CIVETTA J. M., WILLIAMS M. J. and RICHIE R. E. (1970) Diagnostic peritoneal irrigation—a simple and reliable technique. *Surgery* **67**, 874–877.

DE DOMBAL F. T., LEAPER D. U., STANILAND J. R., MCCAIN A. P. and HORROCKS JANE C. (1972) Computer-aided diagnosis of acute abdominal pain. *Br. Med. J.* **2**, 9–13.

GJESSING J., OSKARSSON B. M., TOMLIN P. J. and BROCK-UTNE J. (1972) Diagnostic abdominal paracentesis. *Br. Med. J.* **1**, 617–619.

ROOT H. D., HAUSER C. W., MCKINLEY C. R., LAFAVE J. W. and MENDIOLA R. P. (1965) Diagnostic peritoneal lavage. *Surgery* **57**, 633–637.

SALOMON H. (1906) Die diagnostiche Punktion des Bauches. *Berl. Klin. Wochenschr.* **43**, 45–46.

THAL E. R. and SHIRES G. T. (1973) Peritoneal lavage in blunt abdominal trauma. *Am. J. Surg.* **125**, 64–69.

VEITH F. J., WEBBER W. B., KARL R. C. and DEYSINE M. (1967) Diagnostic peritoneal lavage in acute abdominal disease: normal findings and evaluation in 100 patients. *Ann. Surg.* **166**, 290–295.

Br. J. Surg. Vol. 62 (1975) 121–124

Abdominal lavage in blunt trauma

WILLIAM GILL, HOWARD R. CHAMPION, WILLIAM B. LONG,
JOSEPH JAMARIS AND R. ADAMS COWLEY*

SUMMARY

A technique for abdominal lavage is described and was used to evaluate the abdomen of 671 multiple trauma victims. In 44 per cent (299 cases) there was a bloodstained return and these were regarded as positive. Patients with a positive result underwent exploratory laparotomy which revealed that 89 per cent had significant intra-abdominal trauma requiring a surgical procedure, 8 per cent had trauma which did not require any active surgical correction and 3 per cent had no abnormal findings. Of all the lavages performed, there were 0·11 per cent false positive and 0·03 per cent false negative results. The value of the test in the context of multiple trauma is emphasized.

THE mortality rate in victims of blunt abdominal trauma remains unnecessarily high (Aho and Rasturia, 1971), partly as a result of the perpetuation of inappropriate medical teaching. The classic diagnostic approach of a clinical history proceeding to inspection, percussion, auscultation and palpation followed by special investigations has become almost obsolete in the evaluation of an abdomen in a multiple trauma patient.

Needle abdominal paracentesis described by Neuhof and Cohen in 1926, while clearly a diagnostic advance, was associated with a high number of false negative results (Fitzgerald et al., 1960; Giacobine and Siler, 1960). The introduction of four-quadrant 'tapping' reduced the frequency of false negatives but did not eliminate them (Olsen and Hildreth, 1971). In 1965 Root et al. discussed abdominal lavage as a further diagnostic advance in abdominal trauma, but the technique failed to gain wide acceptance by those dealing with trauma victims.

A slight modification of the technique of Root et al. (1965) has been employed in the Maryland Institute for Emergency Medicine during the past 2 years and the experience gained is described.

Technique of abdominal lavage

1. The bladder is emptied by Foley catheterization.
2. A nasogastric tube is inserted to empty the stomach.
3. A 5 × 7·5 cm area of skin in the midline below the umbilicus is prepared with Betadine solution and draped.
4. One per cent Xylocaine (and adrenaline) is used to infiltrate the midline for approximately 3 cm below the umbilicus and down to the peritoneum.
5. A midline subumbilical incision through skin and subcutaneous tissue is made for 2–4 cm depending on the patient's obesity.
6. Meticulous haemostasis is mandatory and is aided by the adrenaline.
7. The preperitoneal space is entered through the linea alba. If the inferior rectus sheath is entered erroneously the muscle is deflected laterally and an entrance made through the posterior sheath. Improved visualization is obtained by grasping the cut edges of the posterior rectus sheath or linea alba and pulling upwards.
8. The peritoneum is exposed, grasped and tented with two Kelly clamps.
9. After ensuring that no adherent bowel is included in the clamps, a peritoneal purse string suture is placed around the Kelly clamps.
10. A 2–3-mm incision is made in the peritoneum.
11. A standard peritoneal dialysis catheter without the trocar is inserted through this incision into the peritoneal cavity and the purse string suture immediately tightened.
12. The catheter is gently aspirated and an obvious return of blood would obviate further evaluation.
13. If no bloodstained fluid is aspirated, 1000 ml of sterile isotonic crystalloid solution are infused through the catheter by a routine intravenous infusion set. When the intraperitoneal infusion is complete the empty bottle is placed on the floor and the lavage fluid allowed to refill the bottle by gravity.
14. During the infusion the patient should be in a slight Trendelenburg position which is reversed when the infusate is returning to the bottle.
15. The wound is packed with gauze if surgery is to follow or sutured if the result is negative.

Patients

All admissions to the Maryland Institute for Emergency Medicine for the year 1973 were included in the study. During the first 6 months abdominal lavage was performed only for specific indications. Over the latter 6 months the examination was performed on all patients with blunt trauma. The technique described above was rigidly adhered to, and children were lavaged with 500 ml and adults with 1000 ml of crystalloid solution. Penetrating abdominal trauma was excluded from the study because of a different approach to this problem.

When poor technique was recognized as a possible cause of a very faint discoloration in the returning fluid, a second litre of crystalloid solution was infused. Persisting or increasing discoloration in the return from the second bottle was required before the result

---

* Maryland Institute for Emergency Medicine, University of Maryland Hospital, Baltimore, USA.

Table I: NUMBER OF ABDOMINAL LAVAGES PERFORMED IN 1973

	No.	% of total	% of lavages
Trauma admissions	831	100·0	
Lavages performed	671	80·7	100·00
Negative lavages	372		55·23
Positive lavages	299		44·52

Table II: SIGNIFICANCE OF ABDOMINAL PATHOLOGY IN 299 PATIENTS SUBJECTED TO LAPAROTOMY FOR POSITIVE ABDOMINAL LAVAGE

Findings at laparotomy	No.	%
Clinically significant	266	89
Clinically insignificant	25	8
Negative	8	3
Total	299	100

Table III: SIGNIFICANT ORGAN INJURY DETECTED IN 266 PATIENTS SUBJECTED TO LAPAROTOMY FOR POSITIVE ABDOMINAL LAVAGE

Site of injury	No.
Spleen and splenic vessels	107
Liver and hepatic veins	102
Small or large bowel mesenteric vessels	42
Pelvic vessels	38
Large bowel	29
Small bowel	26
Bladder	10
Inferior vena cava	10
Diaphragm	10
Kidney	10
Pancreas	10
Duodenum	5
Gallbladder	5
Stomach	4
Aorta	1
Omental vessels	1
Significant retroperitoneal haematoma	42

Table IV: FALSE RESULTS WITH ABDOMINAL LAVAGE

	No.	% of lavages
Lavages performed	671	
False positive	8	0·110
False negative	2	0·03

was regarded as positive. When poor return of the fluid from the abdominal cavity occurred despite gentle adjustment of the catheter a second litre was also infused.

All patients with bloodstaining of the lavage return were subjected to laparotomy. The intraperitoneal findings were classified as clinically significant when surgical correction or drainage was required, and clinically insignificant when the abnormal findings required no active therapy. A negative laparotomy indicates the total absence of traumatic intraperitoneal pathology and identifies a false positive result.

An analysis was made of some of the factors likely to confuse a clinical attempt to evaluate the abdomen, and related specifically to associated central nervous system and thoracic trauma and the presence of alcohol in the blood.

No attempt was made to correlate the clinical findings with the lavage results and eventual pathology or to correlate the degree of staining of the lavage return with the intra-abdominal pathology, as described by Olsen et al. (1972).

Results

In the 12-month period studied, 943 patients were admitted to the Maryland Institute for Emergency Medicine of which 831 (88 per cent) were trauma victims transferred directly from the scene of the accident or from another hospital. Six hundred and forty-one (68 per cent) of these admissions arrived by helicopter. Abdominal lavage was performed in 671 patients to exclude traumatic intraperitoneal pathology. Three hundred and seventy-two (55·23 per cent) were found to be negative and 299 (44·52 per cent) positive (*Table I*). The latter 299 patients were subjected to exploratory laparotomy. In 266 (89 per cent) there were surgically significant lesions, and 8 (3 per cent) were negative (*Table II*). The clinically significant findings are listed in *Table III*. Twenty-five (8 per cent) patients had clinically insignificant findings at laparotomy. False negatives occurred in 2 instances (*Table IV*).

Of the 831 trauma admissions, 50 per cent showed alcohol in their blood on arrival and 25 per cent had over 0·15 mg/100 ml (the upper legal limit for driving in Maryland). Three hundred and forty-nine patients sustained central nervous system (CNS) injury with impaired consciousness, and 132 (38 per cent) of these required laparotomy for abdominal trauma. Almost half (44 per cent) of the patients with abdominal injury had a CNS injury. Two hundred and twenty-one patients sustained a thoracic injury and 124 were submitted to exploratory laparotomy. Thoracic trauma was present in 41 per cent of patients with abdominal injury, and 56 per cent of all the patients with thoracic injury underwent laparotomy. Multiple trauma involving the thorax, central nervous system and abdomen occurred in 50 patients; only 38 patients had isolated abdominal trauma, and 65 per cent of all the trauma patients had one or more fractures.

Discussion

Mortality from abdominal trauma is related not only to the severity of the injury and associated trauma but also to delay in diagnosis (Williams and Zollinger, 1959; McLeod and Brown, 1966; Bolton et al., 1973). The difficulties of clinical diagnosis in the presence of head injury, alcoholic intoxication (Williams and Zollinger, 1959; Nicholson and Golden, 1966) and extra-abdominal trauma (Macbeth, 1966; Olsen and Hildreth, 1971) are well described.

In the Institute's special admitting areas, abdominal evaluation is limited to abdominal lavage after a cursory inspection for visible expansion. Radiological examination of the abdomen is not performed routinely and haemodynamic stabilization of the patient is clearly a priority. Because abdominal lavage is a routine part of our initial resuscitative and diagnostic effort, the mortality and morbidity related to delay in diagnosis are effectively removed. Meticulous technique in the performance of the lavage is essential for accuracy, and visceral damage is avoided by elevating the peritoneum before making the incision. A crystal-clear return of lavage fluid is the only confirmation of a technically perfect lavage, and bloodstaining of the fluid means that blood from the incision has entered the peritoneal cavity during the catheter insertion or that intraperitoneal bleeding is present. Poor technique accounted for all our false positive results.

Twenty-five (8 per cent) of our patients had exploratory laparotomy findings not requiring any further surgical procedure. Twenty of these had mildly positive lavage results, although the remainder showed deeper staining of the effluent.

Various attempts to increase the accuracy of abdominal lavage include gradations based on red and white blood cell counts in the fluid, amylase estimations (Perry and Strak, 1972) and the presence of ammonia (Mansberger et al., 1959) to mention a few. We have found such scales to be too time-consuming in an emergency situation and to provide no useful additional information. Very weakly bloodstained lavage fluid not infrequently indicates a bowel perforation with minimal bleeding from the edges of the hole or may be the only clue to a ruptured duodenum or other retroperitoneal injury. It is for this reason that all bloodstained lavage results are regarded as an indication for exploratory laparotomy. In this context the deliberate acceptance of a number of exploratory laparotomies revealing 'clinically insignificant' pathology is necessary just as the negative laparotomy is acceptable in other situations when it is used as the final diagnostic manœuvre. If anything, its use in the management of trauma is more essential because of the detrimental effect of delay in treatment.

Constructive attention should be directed towards the false negative results obtained rather than the false positives because it is in these patients that a delay in diagnosis is likely to increase the mortality and morbidity. It is possible that previous surgery in the abdomen may result in the isolation of an injured viscus by fibrous adhesions and prevent adequate distribution of the instilled crystalloid solution. The presence of healed abdominal scars should consequently stimulate the surgeon to consider an alternative site for the lavage incision, and to agitate or promote movement of the abdomen to ensure good circulation of the fluid. The surgeon must also be wary of the potential danger of bowel perforation during the intraperitoneal introduction of the catheter.

Trauma confined to the retroperitoneal space can never be excluded with certainty by abdominal lavage (Olsen and Hildreth, 1971), but to date this has not been a problem in our patient population. This may be related to the fact that the magnitude of trauma required to injure retroperitoneal structures produces associated intraperitoneal trauma which is detected by the lavage. In our experience, retroperitoneal hematomas almost always stain the lavage fluid even though covered by intact peritoneum.

The 2 false negative results reported were patients in whom rupture of the left hemidiaphragm was apparent on chest X-ray, with translocation of the stomach, colon and spleen into the chest. Both underwent laparotomy despite negative lavages, and in both instances splenic rupture was present. In one patient 500 ml of blood were found in the thoracic cavity without spillage into the abdominal cavity—a presumed result of the herniation and negative intrathoracic pressure. The ruptured diaphragm thus presents a further weak area for lavage diagnosis, though it is unlikely to occur unless there has been a major disruptive force and other visceral injury, or to escape detection on chest X-rays.

Abdominal lavage is still confused with abdominal 'taps' in the minds of many surgeons despite the ever increasing reports in the literature clarifying the procedure. Mis-statements in medical texts are numerous and reflect the inadequate experience of the authors in many cases. It has been stated that as little as 200 ml of blood in the peritoneal cavity may be detected by lavage when quite clearly a few drops of blood introduced at the time of incision will give a false positive result.

At present, we rely almost entirely on this procedure for our initial evaluation of the abdomen in blunt trauma victims and have had no cause for regret. We feel that knowledge of the value of this tool is lost in the midst of long descriptions of how to examine and assess the abdomen in this type of patient and that current texts have not yet fully appreciated the real value or import of the test. The time is overdue for change however much it saddens the traditional diagnostician's heart.

Acknowledgements

This work was supported by grants from the US Army Material Systems Analysis Agency DAAD 05-73-C-0032, and from the Office of the Surgeon General, US Army 3A 16 2110A821.

References

AHO A. J. and RASTURIA R. D. (1971) Closed abdominal injury. Observations of changes in material and activation of treatment. *Acta Chir. Scand.* **137**, 429–435.

BOLTON P. M., WOOD C. B. and QUARTEY-PAPATIA J. D. (1973) Blunt abdominal injury: a review of 59 consecutive cases undergoing surgery. *Br. J. Surg.* **60**, 657–663.

FITZGERALD J. D., CRAWFORD E. S. and DEBAKEY M. D. (1960) Surgical consideration of non-penetrating abdominal injuries: an analysis of 200 cases. *Am. J. Surg.* **100**, 22–29.

GIACOBINE J. W. and SILER V. E. (1960) Evolution of diagnostic abdominal paracentesis with experimental and clinical studies. *Surg. Gynecol. Obstet.* **110**, 676–686.

MACBETH R. A. (1966) Blunt abdominal trauma. *Can. J. Surg.* **9**, 384–396.

MCCLEOD R. A. and BROWN D. R. (1966) Non-penetrating abdominal trauma. *Can. J. Surg.* **9**, 379–383.

MANSBERGER A. R. jun., COWLEY R. A., BESSMAN S. P. and BUXTON R. W. (1959) The origin and utilization of ammonia in strangulation obstruction of the small bowel. *Ann. Surg.* **150**, 880–889.

NEUHOF H. and COHEN L. (1926) Abdominal puncture and diagnosis of acute intra-peritoneal disease. *Ann. Surg.* **83**, 454–462.

NICHOLSON R. and GOLDEN G. (1966) Blunt abdominal trauma in head injuries. *Lancet* **2**, 793–794.

OLSEN W. R. and HILDRETH D. H. (1971) Abdominal paracentesis and peritoneal lavage in blunt abdominal trauma. *J. Trauma* **11**, 824–829.

OLSEN W. R., REDMAN H. C. and HILDRETH D. H. (1972) Quantitative peritoneal lavage in blunt abdominal trauma. *Arch. Surg.* **104**, 536–543.

PERRY J. F. jun. and STRAK R. G. (1972) Diagnostic peritoneal lavage in blunt abdominal trauma: indications and results. *Surgery* **71**, 898–901.

ROOT H. D., HAUSER C. W. and MCKINLEY C. R. (1965) Diagnostic peritoneal lavage. *Surgery* **57**, 633–637.

WILLIAMS R. D. and ZOLLINGER R. M. (1959) Diagnostic and prognostic factors in abdominal trauma. *Am. J. Surg.* **97**, 575–578.

Why run the risk of her cystitis ascending, and the problem of pyelonephritis developing? Rapid, effective therapy with SEPTRIN is indicated at the first opportunity.

SEPTRIN was rated top oral treatment in a British survey of 23,491 urinary pathogen sensitivities.[1] SEPTRIN has been judged superior to ampicillin[2,3] and is now well established as a first-line treatment for urinary infections.

SEPTRIN contains trimethoprim and sulphamethoxazole. Full prescribing information is available on request.

Wellcome

1 *Postgrad med J.* (1971) **47**, Supplement (September), 7.
2 *Brit med J.* (1972) **2**, 673.
3 *Clin Trials J.* (1972) **9/3**, 9.

Wellcome Medical Division,
The Wellcome Foundation Ltd.,
Berkhamsted, Herts.

SEPTRIN
TRADE MARK

Trauma Surgery: Excepting Bones and Joints

P. POWLEY, MB, BS, FRCSE, FRCS

Consultant Surgeon,
Swindon and District Hospital Group

136 pages 18 illustrations Paper covers £1·50 net

Common Surgical Emergencies

C. B. WILLIAMS, MD, FRCS

Senior Registrar in General Surgery,
United Bristol Hospitals

156 pages 3 illustrations Paper covers £1·50 net

Electrocardiograms: A Systematic Method of Reading Them

3rd Edition

MICHAEL L. ARMSTRONG, MB, BS

80 pages 84 illustrations Paper covers £2·00 net

The Principles of Transurethral Resection and Haemostasis

J. P. MITCHELL, TD, MS, FRCS, FRCSE

Lecturer in Urology, University of Bristol;
Consultant Urological Surgeon,
United Bristol Hospitals

176 pages 124 illustrations £6·00 net

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

Br. J. Surg. Vol. 62 (1975) 125–129

Extrinsic duodenal obstruction in infants and children

G. TRYFONAS AND D. G. YOUNG*

SUMMARY

A series of 34 patients with extrinsic duodenal obstruction is described. The diagnosis and treatment are discussed. Five infants died and the findings are given. The remaining 29 have progressed normally.

DUODENAL obstruction in a newborn infant was first described by Calder (1733), and Ernst (1916) was the first to report its successful treatment. Subsequently, it became apparent that there were two types of neonatal duodenal obstruction. The cause of intrinsic duodenal obstruction (atresia, membrane or severe stenosis) was clearly defined in the nineteenth century, but the cause of extrinsic duodenal obstruction due to Ladd's bands or volvulus of the midgut was first described by Dott (1923). Extrinsic duodenal obstruction may also occur in later infancy and childhood because of compression of the third portion of the duodenum by the superior mesenteric artery.

Higgins (1923) first reported a successful operation on an infant with extrinsic duodenal obstruction. The operative approach described by Ladd (1937) has become generally accepted as the best treatment at any age for extrinsic duodenal obstruction (Louw, 1960). Details of series of patients with extrinsic duodenal obstruction are remarkably scanty, with the main report coming from Boston (Gross, 1953) and another from London (Young and Wilkinson, 1966). A study of 34 infants and children with extrinsic duodenal obstruction is presented here.

Patients

The case records of 34 infants and children presenting with signs or symptoms which were proved to be due to extrinsic duodenal obstruction and who were admitted to the surgical wards at the Royal Hospital for Sick Children, Glasgow, between 1966 and 1973 have been reviewed.

Age and sex

On admission the ages of the patients varied from 1 day to 11 years. Twenty-eight were admitted in the neonatal period and the mean age on admission was 6·8 days. The remaining patients were admitted at the age of 5 months, 7 months, 2, 3, 5 and 11 years. There was an equal sex distribution.

Pregnancy and birth weight

In none of the 31 pregnancies of which details were known had hydramnios occurred. Two infants were born before the 36th week. One infant had a birth weight of 1·56 kg and the remainder weighed from 2·5 to 4·5 kg.

Clinical features

All the neonates showed signs of an upper intestinal obstruction. All the patients had vomited bile-stained fluid. The vomiting did not always continue. In some it subsided and returned only weeks or months later. In 2 patients bile-stained vomiting had been episodic over years and this had given rise to difficulty in making a diagnosis. Only 2 infants failed to pass meconium and most had passed changed stools. In the older infants and children bowel habit had been normal until the acute episode, except in 1 child who had been constipated until the age of 3 years. He then had an acute episode of severe abdominal pain and bile-stained vomiting.

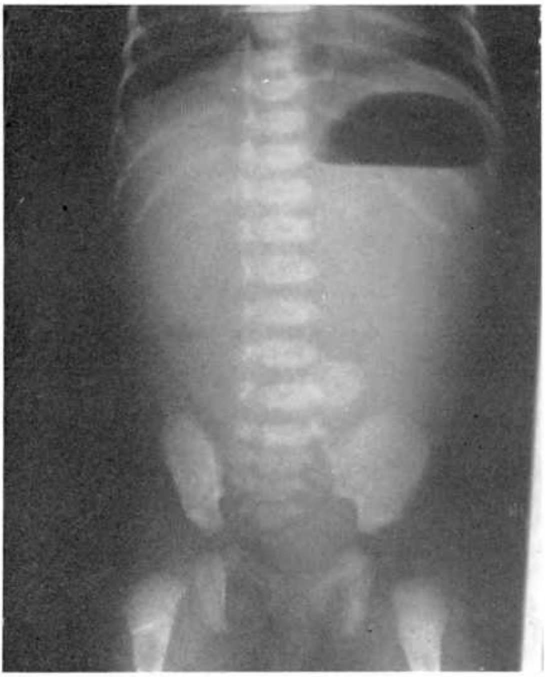
Diagnosis

Bile-stained vomiting should always arouse the suspicion of intestinal obstruction, but in the neonatal period there are other causes of bile-stained vomiting. Unlike intrinsic duodenal obstruction, X-rays of the abdomen in the erect posture were not always helpful in making the diagnosis of extrinsic duodenal obstruction. An abnormal but variable pattern of gas distribution throughout the gut with fluid levels in the stomach, and sometimes in the duodenum and the small bowel when volvulus had occurred, were the most common findings; lack of the normal distribution of gas throughout the gut of an infant is also significant (*Fig.* 1). As the obstruction of the duodenum is acute, proximal dilatation of the duodenum is not marked and so the 'double bubble' sign found in the longer standing intrinsic obstruction may not be seen. When straight X-rays did not clarify the position radiological studies using a contrast medium (e.g. barium sulphate or Gastrografin) were made to define the anatomical arrangement. This was given orally (*Fig.* 2) or instilled into the large bowel.

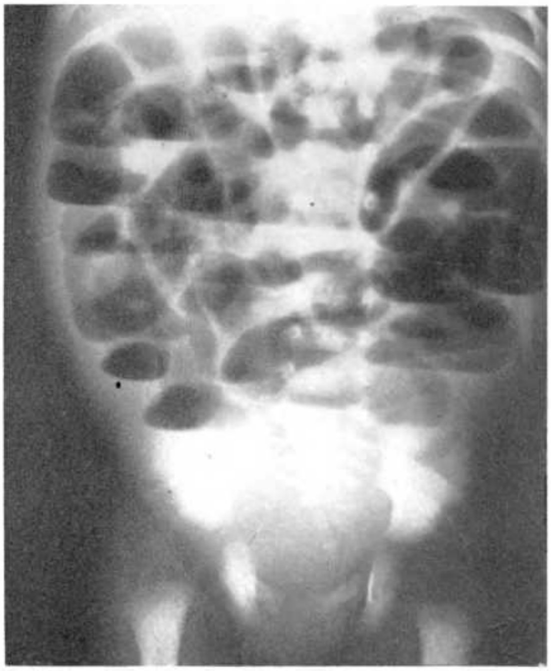
In the infants or children with malrotation the duodenojejunal flexure was displaced to the right and the proximal small bowel was lying predominantly on the right side of the peritoneal cavity rather than on the left. Follow-through studies demonstrated the abnormal position of the proximal large bowel (*Fig.* 3). Barium enema examination was used on occasion to define the malrotation of the bowel. Rather than a barium enema, the technique recommended by Rickham (1969) of filling the large bowel with air can delineate the large bowel and caecum. The normal position of the large bowel does not exclude extrinsic duodenal obstruction, and 2 neonates with volvulus of the small bowel with a normally rotated colon were treated.

---

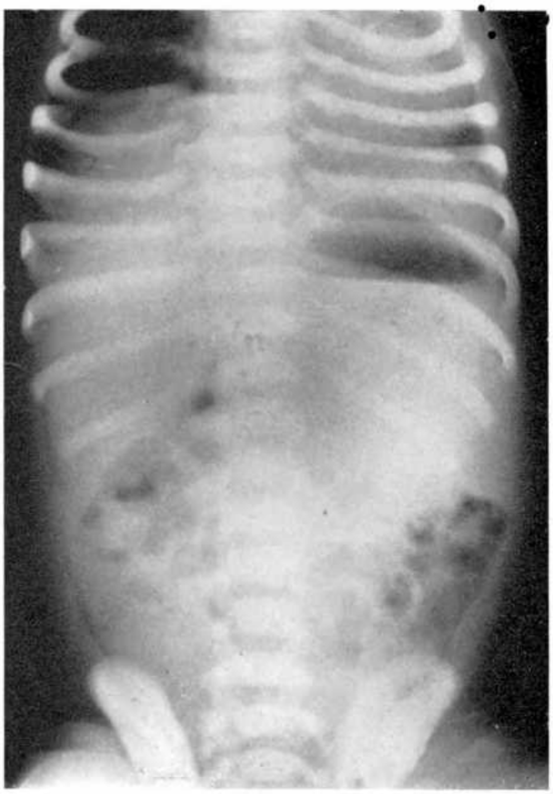
* Royal Hospital for Sick Children, Glasgow.



a



c



b

Fig. 1. *a*, Straight X-ray showing fluid level in the stomach and very little gas in the small bowel. The infant had extrinsic obstruction with volvulus. *b*, Fluid level in the stomach. Abnormal distribution of gas in an infant with malrotation and Ladd's bands, and suspected intermittent volvulus. *c*, Grossly abnormal gas distribution in the gut with multiple fluid levels in an infant with volvulus.

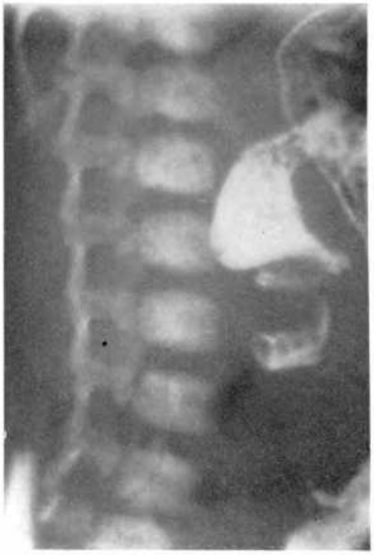


Fig. 2. Barium meal film showing a dilated duodenum which is constricted in the lower part due to extrinsic pressure from bands. Note: There is not the gross proximal dilatation seen with intrinsic obstruction.

Pathological anatomy

Extrinsic duodenal obstruction usually falls into one of three groups, but a mass compressing the duodenum can cause obstruction. During the period under review no such patient was admitted.

Type A. Malrotation with bands

The term 'malrotation' is widely used when the midgut does not complete the normal process of

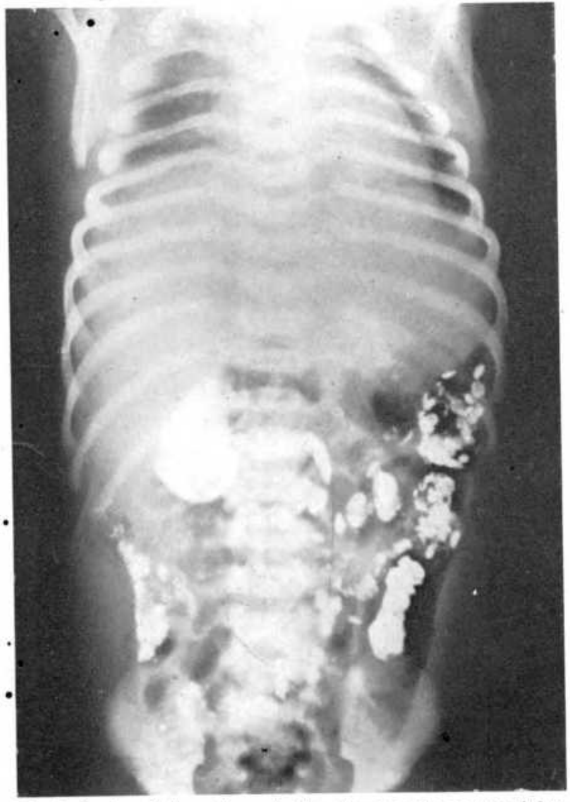


Fig. 3. Barium follow-through film showing the caecum lying in the midline.

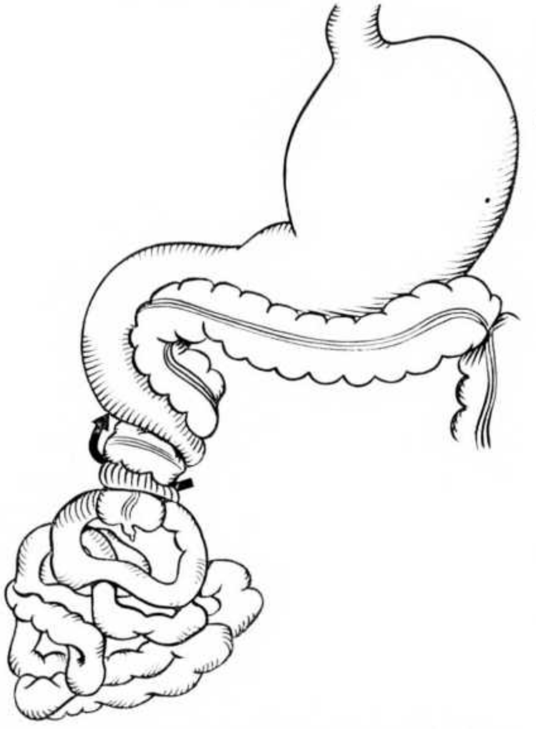


Fig. 5. Diagrammatic representation of malrotation with volvulus.

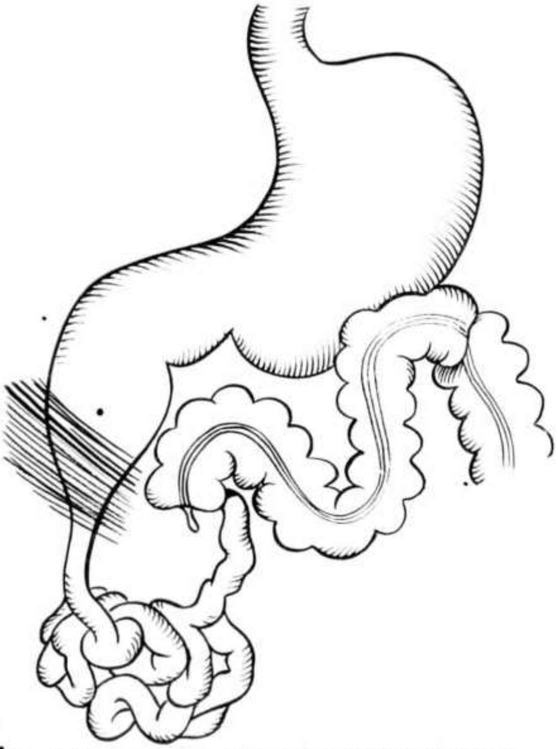


Fig. 4. Diagrammatic representation of malrotation with Ladd's bands obstructing the duodenum.

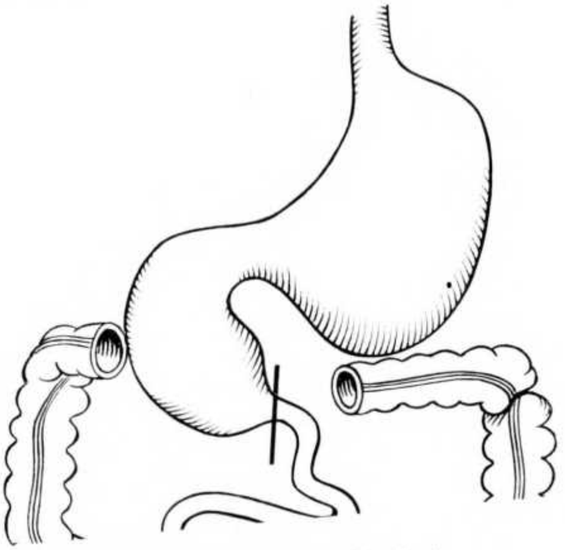


Fig. 6. Diagrammatic representation of duodenal obstruction due to superior mesenteric vessels.

rotation and fixation in utero. With this incomplete rotation the duodenum fails to cross the midline to the normal duodenojejunal junction at the ligament of Treitz. The caecum fails to rotate across the midline and down into the right iliac fossa, and from the caecum peritoneal 'bands' spread to the posterior abdominal wall and sometimes to the gallbladder and undersurface of the liver. These bands cross the duodenum and in 17 patients in the present series were the cause of the obstruction (*Fig.* 4). The obstruction usually began a few days after birth when the colon becomes more active. The bands are pulled across the descending duodenum distal to the entrance of the bile ducts.

Type B. Malrotation with volvulus of the midgut

With incomplete rotation of the gut the base of the mesentery is narrow. This allows the midgut loop to twist upon itself (*Fig.* 5). Thirteen patients in the present series had volvulus of the midgut loop, and a further 2 had complete rotation of the large bowel but incomplete rotation of the duodenum and had volvulus of the proximal part of the midgut loop. This type of obstruction was mentioned by Wilkinson (1973). When volvulus supervenes the mesenteric vessels may be obstructed and cause infarction of the bowel. Two infants in the present series had extensive gangrene of the bowel and a third had incipient gangrene with the bowel about to perforate at the time laparotomy was performed.

Type C. Superior mesenteric artery obstruction, also referred to as 'duodenal ileus'

This third type of obstructing lesion of the duodenum is uncommon and occurred in 2 infants in this series (*Fig.* 6). The duodenum passes behind the superior mesenteric vessels which press on the duodenum and may cause obstruction which is always incomplete. The patients may adopt unusual postures, particularly after meals, to relieve the pressure of the mesenteric vessels on the duodenum. This apparently bizarre behaviour may lead one to suspect psychiatric disease, but the relief of the obstruction by postural alteration can be demonstrated at radiological screening.

Treatment

The operative correction in all the patients of this series (including the 2 with obstruction due to the superior mesenteric vessels) was basically the procedure described by Ladd (1937). The abdomen was usually opened through a transverse incision and the peritoneal cavity explored. The caecum and proximal colon were then mobilized by dividing the bands extending from these organs. The large bowel was displaced to the left side of the abdomen and in doing so the base of the mesentery was gradually broadened. Any rotation of the duodenum towards the left was undone so that the duodenum ran down the right paravertebral gutter into the proximal jejunum on the right. Fluids were usually administered by intravenous infusion for 48 hours after operation, when oral feeding was started. The appendix was removed from 12 of the patients in this series. Where volvulus had been present or when there was any doubt about the viability of the bowel, additional procedures such as appendicectomy were avoided.

Results

Five patients died, 1 just after admission and 4 during the first 24 hours after operation. Necropsies were permitted in 4 of the 5 patients who died. In 2 no precise cause of death was found. An unusual incidental finding in one of these was pneumatosis of the bladder. Bacteriological culture was negative and the lack of an inflammatory reaction in the submucosa of the bladder was against this being of infective origin.

In 1 infant mucopurulent material was present in the bronchi, the bronchopneumonia contributing to the fatal outcome, but it was felt that aspiration of a small quantity of vomit was the primary cause of the death. In another infant death was due to widespread staphylococcal infection. Two patients had gangrene of the bowel. The infant whose parents refused necropsy weighed only 1·56 kg and suffered from repeated apnoeic attacks following operation. It was presumed that death was the result of an apnoeic attack.

Discussion

The factors which interrupt the normal rotation of the gut remain obscure. In only one of the present series was a clear aetiological factor present. This baby was admitted on the first day of life with a left diaphragmatic hernia. Operation was carried out to repair the hernia but 1 week after the operation he started to vomit bile-stained fluid. A laparotomy was carried out and Ladd's (1937) procedure was performed to correct the malrotation of the gut with bands which crossed the junction of the second and third parts of the duodenum.

A low incidence of associated abnormalities has been reported (Young and Wilkinson, 1968). In the present series, apart from the diaphragmatic hernia, there was no other serious congenital malformation but 1 infant was small and premature. Aitken (1966) has stressed the frequency of malrotation complicating intrinsic duodenal obstruction. All patients with intrinsic duodenal obstruction and malrotation have been excluded as the former was the primary cause of obstruction. The lack of patients with anomalies such as exomphalos or diaphragmatic hernia could be due to the latter conditions being treated within a few hours of birth. In both conditions laparotomy is usually performed and if duodenal bands likely to cause obstruction are present, these are divided. It has not been the author's experience to find potentially obstructive bands with these malformations.

Diagnosis of extrinsic duodenal obstruction depends on being aware of it as a possibility. When an infant has been feeding and then suddenly develops bile-stained vomiting an organic cause for this should be sought. Speed is essential as there is no external evidence to indicate which infants have volvulus (type B). This complication requires immediate correction as delay may result in gangrene of the small bowel. In 1 of the 15 type B cases the bowel was on the point of perforating at the time of laparotomy and delay for a few hours would have resulted in faecal peritonitis, and in 2 cases gangrene had supervened and both these patients died. Types A and C obstruction do not require urgent operation. It is

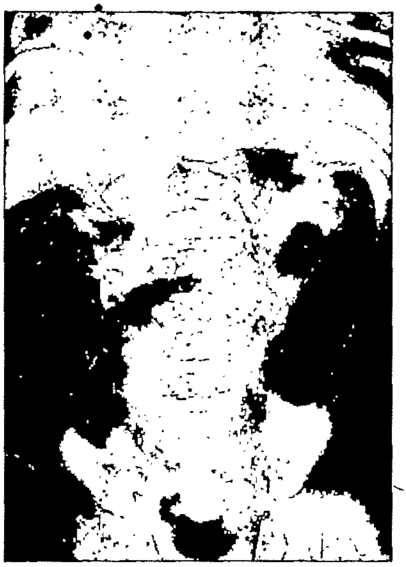


Fig. 7. Straight X-ray showing the small bowel on the right and large bowel on the left. Malrotation was confirmed subsequently at laparotomy for other reasons but the infant never had any signs of obstruction.

impossible in some cases to define whether the infant has type A or B obstruction from clinical or simple radiological investigations and these infants require urgent attention to prevent the bowel becoming gangrenous. Radiological evidence of extrinsic obstruction has already been shown to be variable. The danger is that the straight X-ray may not show any dramatic evidence of the duodenal obstruction and the diagnosis is missed. It must also be remembered that a contrast enema does not exclude volvulus of the small bowel which occasionally causes extrinsic duodenal obstruction. Radiological examination may show malrotation (*Fig.* 7), but the child may not require any active treatment. Warkany (1971) stated that 50 per cent of patients with malrotation do not require operation. All the patients in the present series were considered to require operation as they presented with signs of extrinsic duodenal obstruction.

The intermittent nature of duodenal obstruction of types A and C in some patients also causes difficulty in diagnosis. In the older boy with type C obstruction the bizarre positions that he adopted to relieve his obstruction and the periodic nature of the vomiting gave rise to the question of psychiatric disease. The same error has occurred in adults with this disorder. Diagnosis can be made only by barium meal examination. Louw (1960) indicated the improved results of the Ladd (1937) approach to the superior mesenteric artery obstruction. Other operations such as gastro- or duodenojejunostomy have only 'cured' about 2 of every 3 patients with this type of obstruction.

The danger of even a very small vomit or regurgitation in an infant cannot be overstressed and close immediate postoperative care is essential to prevent avoidable mortality. A significant fact was that all the infants, except the small premature baby, died during the night. In 2 if not 3 of the deaths it was felt that continuous supervision with immediate availability of experienced help, as is now routine, would have prevented the deaths. Unlike intrinsic duodenal obstruction, where there is a high mortality due to associated abnormalities, the extrinsic duodenal obstruction is usually an isolated defect.

Acknowledgments

We wish to thank the surgeons at the Royal Hospital for Sick Children, Glasgow, for permission to review their patients, and the nursing staff of the hospitals at which we have treated these infants for their care and attention.

References

AITKEN J. (1966) Congenital intrinsic duodenal obstruction in infancy. *J. Paediatr. Surg.* **1**, 546–558.

CALDER J. (1733) Two examples of children born with preternatural conformations of the guts. *Med. Essays Observations Edinb.*, 5th ed. **1**, 165–167.

DOTT N. M. (1923) Anomalies of intestinal rotation; their embryology and surgical aspects with report of 5 cases. *Br. J. Surg.* **11**, 251–286.

ERNST N. P. (1916) A case of congenital atresia of the duodenum treated successfully by operation. *Br. Med. J.* **1**, 644–645.

GROSS R. E. (1953) *The Surgery of Infancy and Childhood.* Philadelphia, Saunders, p. 202.

HIGGINS T. T. (1923) A case of intestinal obstruction in a newborn infant. *Br. J. Surg.* **11**, 382–384.

LADD W. E. (1937) Congenital duodenal obstruction. *Surgery* **1**, 878–885.

LOUW J. H. (1960) Intestinal malrotation and duodenal ileus. *J. R. Coll. Surg. Edinb.* **5**, 101–126.

RICKHAM P. P. (1969) *Neonatal Surgery.* London, Butterworths, p. 310.

WARKANY J. (1971) *Congenital Malformations.* Chicago, Year Book Medical Publishers, p. 692.

YOUNG D. G. and WILKINSON A. W. (1966) Mortality in neonatal duodenal obstruction. *Lancet* **2**, 18–20.

YOUNG D. G. and WILKINSON A. W. (1968) Abnormalities associated with neonatal duodenal obstruction. *Surgery* **63**, 832–836.

WILKINSON A. W. (1973) Congenital causes of duodenal obstruction. *J. R. Coll. Surg. Edinb.* **18**, 197–208.

Br. J. Surg. Vol. 62 (1975) 130–134

Carcinoma of the pancreas and periampullary region: a clinical study in a district general hospital

D. J. T. WEBSTER*

SUMMARY

One hundred patients with pancreatic and periampullary carcinoma have been reviewed. Diabetes mellitus may be an early presentation. Painless jaundice has a relatively good prognosis. Fifteen patients have had curative procedures with a 31 per cent operative mortality. Mortality is influenced by age and serum bilirubin levels. Where palliative procedures are undertaken, this should include biliary diversion and gastro-enterostomy.

CARCINOMA of the head of the pancreas accounts for about 2500 deaths per year in England and Wales (Registrar General, 1971). The death rate seems to be increasing (Krain, 1970). No aetiological factor has been determined, although Wynder et al. (1973) have recently reported an attractive concept related to carcinogen excretion in the bile.

Most papers in the past have come from large centres with a special interest in the problem of pancreatic cancer. The figures from these series are therefore not representative of the disease as it affects the general population. This review was undertaken to assess the influence of treatment on the course of the disease in a district general hospital and in particular to define the place of radical surgery. Carcinomas of the ampulla and distal part of the bile duct have been included because even at operation it may be difficult to distinguish between them and carcinomas of the head of the pancreas.

Patients and methods

A diagnostic index recorded 108 patients as having pancreatic, bile duct or ampullary carcinoma between 1 January 1958 and 31 December 1972. Tumours of the upper biliary tree and gallbladder have been excluded.

Eight patients were excluded from this study, 5 because there was insufficient documentation and 3 because the diagnosis was subsequently revised on the basis of histological examination to hepatocellular carcinoma, benign cystadenoma of the pancreas and chronic pancreatitis respectively.

Operative death is defined as occurring within 1 month of operation or before discharge from hospital.

The sites of origin of the carcinoma are shown in *Table I.* The mean age of these patients was 63 years with an age range of 35–87. There were 52 men and 48 women.

On the basis of surgical management, the patients have been divided into three groups (*Table II*): 'radical' surgery is defined as excision of the tumour with a view to cure; 'palliative' surgery refers to bypass procedures of the biliary and/or gastro-intestinal tracts; the 'no treatment' group had either an exploratory laparotomy only or no operation at all. None of the patients was treated by radiotherapy or chemotherapy.

Table I: SITES OF ORIGIN OF CARCINOMA

Diagnosis	No. of cases	
Carcinoma of head of pancreas	75	92
Carcinoma of body and tail of pancreas	17	
Carcinoma of ampulla of Vater		4
Carcinoma of lower end of bile duct		4
Total		100

Table II: LENGTH OF PREOPERATIVE SYMPTOMS BY TREATMENT GROUP

		Length of preop. symptoms (mth)		Age (yr)	
Treatment	No.	Mean	Range	Mean	Range
Radical	15	3·5	1–12	59	40–75
Palliative	56	3·5	1–36	65	41–87
No treatment	29	7·1	1–24	63	35–85
Total	100	4·3	1–36		

Table III: PRESENTING SYMPTOMS

Presenting symptom	No.*	Total No.†
Pain	46	57
Jaundice	33	72
Anorexia and weight loss	14	49
Vomiting	5	
Bowel disturbance	2	
Mass	1	1
Psychosis	0	1

* Number with this symptom as first or leading complaint.
† Total number in the series with this symptom.

Findings

Presenting symptoms

The presenting symptoms are shown in *Table III.* Painless jaundice occurred in 38 patients and 11 of these had a radical procedure. In the remaining 27 patients 17 had definite evidence of unresectability. In 10 patients no assessment was recorded and a palliative procedure was performed.

The average duration of symptoms before operation is shown in *Table II.* There was no difference between the patients having radical or palliative procedures. The no treatment group had symptoms for twice as long before seeking medical advice. Patients with tumours of the body and tail of the pancreas had symptoms for longer (mean 8 months) compared with those with carcinoma of the head (mean 3 months). They more frequently fall into the no treatment group because of the position of the tumour.

---

* St Woolos' Hospital, Newport, Monmouthshire.
Present address: University Department of Surgery, Welsh National School of Medicine, Heath Park, Cardiff CF4 4XN.

Associated diseases

The associated diseases are shown in *Table IV*. Fifteen patients were found to have diabetes mellitus either at presentation or up to 8 years previously. Glucose tolerance tests were not performed routinely. Six patients had had diabetes mellitus for more than 3 years and 4 of these had become unstable shortly before symptoms of carcinoma appeared. There is no significant correlation between the site of the carcinoma and the occurrence of diabetes. Diabetes mellitus occurred in 17 per cent of head lesions and 20 per cent of body/tail lesions.

Cholelithiasis occurred in 14 patients. Six of these patients had had cholecystectomies from 2 to 20 years previously. In the other 8 patients the stones were incidental findings at the time of laparotomy, although in 1 case there were numerous stones in the common bile duct.

Ulcerative colitis occurred in 2 female patients aged 59 and 65 years. This diagnosis had been made on clinical, radiological and histological assessment and in both cases had been present for between 10 and 15 years. Neither had had a colectomy. One had a recurrence of diarrhoea associated with jaundice and a palpable gallbladder. The other patient presented with abdominal pain radiating to the back and associated with jaundice, with no associated symptoms of colitis.

Operations

In the no treatment group 21 patients out of 29 had a laparotomy to confirm the diagnosis.

Fifty-six patients had a palliative procedure performed. The type of operation used is shown in *Table V*. Fifteen patients underwent radical surgery; 13 of these had a partial pancreaticoduodenectomy. The mean age of this group was 58·5 years (range 40–75) and some details of these patients are summarized in *Table VI*. The usual mode of reconstruction was end-to-end choledochojejunal anastomosis, an end-to-side pancreaticojejunostomy and a gastroenterostomy distal to these anastomoses. Neither antrectomy nor vagotomy was carried out as a routine. One patient had a two-stage procedure.

Results of treatment

No treatment group

There were 29 patients in this group who had a mean disease duration (from first symptom to death) of 9 months. The mean survival after diagnosis was 2 months. Twelve patients had tumours in the body or tail of the pancreas. The other 17 patients had

Table IV: ASSOCIATED DISEASES

Disease:	No.:
Diabetes mellitus	15
Cholelithiasis	14
Ulcerative colitis	2
Peptic ulcer	2

Table V: PALLIATIVE PROCEDURES USED

		Operative	mortality
Procedure	No.	No.	%
Cholecystoduodenostomy	32 (2)	3	10
Choledochoduodenostomy	10 (1)	5	50
Cholecystojejunostomy	7 (1)	2	30
Choledochojejunostomy	2	1	50
External T-tube drainage	2	2	100
Gastro-enterostomy	3 (3)	0	0
Total	56 (7)	13	25

The numbers in parentheses show those who had gastro-enterostomy performed as part of the first operation.

Table VI: COMPLICATIONS FOLLOWING PALLIATIVE SURGERY

Complication:	No.:	%:
Duodenal obstruction	12	26
Recurrent jaundice	3	7
Biliary fistula	2	4
Wound dehiscence	2	4
Wound infection	2	4
Subphrenic abscess	1	2

Table VII: DETAILS OF PATIENTS HAVING PANCREATICODUODENECTOMY

Diagnosis	Sex	Age (yr)	Bilirubin (mg %)	Result	Comment
Carcinoma of head of pancreas	M	66	20	Operative death	Necrotic pancreatic anastomosis
Carcinoma of head of pancreas	M	57	16	Alive and well at 20 mth	Steatorrhoea
Carcinoma of head of pancreas	M	40	11	Died at 8 mth	Recurrent cancer
Carcinoma of head of pancreas	F	71	11	Alive and well at 12 mth	
Carcinoma of head of pancreas	F	73	15	Operative death	Bleeding from portal vein
Carcinoma of head of pancreas	F	59	7	Died at 13 mth	Recurrence
Carcinoma of head of pancreas	F	75	21	Operative death	Died on day 5. No post-mortem
Carcinoma of head of pancreas	M	57	11	Died at 5 mth	Recurrence
Carcinoma of bile duct	M	48	15	Operative death	Pulmonary embolus on day 19
Carcinoma of bile duct	M	50	8	Alive and well at 22 mth	
Carcinoma of bile duct	M	56	11	Died at 18 mth	Recurrence
Carcinoma of ampulla	F	62	2	Alive and well at 40 mth	Two-stage procedure. Initial bilirubin 14 mg %
Carcinoma of ampulla	M	57	9	Died at 9 mth	Recurrence

Table VIII: SERUM BILIRUBIN AND AGE OF PATIENTS UNDERGOING RADICAL SURGERY

Patients	No.	Bilirubin (mg %) Mean	Bilirubin (mg %) Range	Age (yr) Mean	Age (yr) Range
Survived	9	10	2–16	55	40–71
Died	4	18	10–21	65	48–75
Total	13	12·5		59	

tumours in the head of the pancreas. There was no difference in the length of symptoms before diagnosis or in duration of disease between these two sites.

Palliative group
The 56 patients in this group had a mean survival of 11 months from the first symptom, or 8 months from operation. No patient in this group is still alive, only 7 (13 per cent) survived for 1 year and 1 (2 per cent) for 2 years following operation. Four out of 12 patients with hepatic deposits at operation survived for a further 6 months.

The operative mortality was 23 per cent. The mean age of the patients who died was 71 years, compared with 63 in those who survived.

Complications following palliative surgery are shown in *Table VII*. The most significant of these complications was the subsequent appearance of duodenal obstruction. Out of 49 patients at risk, 7 (14 per cent) had a subsequent laparotomy for symptoms of duodenal obstruction. All were improved by a gastro-enterostomy. A further 6 patients died with symptoms suggestive of duodenal obstruction. The onset of these symptoms was from 1 to 13 months after the biliary diversion but usually between 4 and 6 months. Most of these patients had had disease confined to the pancreas at the initial laparotomy but 2 had had peritoneal deposits and 2, hepatic deposits. One of the 7 patients having a gastro-enterostomy as a second procedure died before leaving hospital. The remainder lived, free of obstructive symptoms, for between 2 and 12 months. Although vagotomy was not carried out, no patient had subsequent symptoms of anastomotic ulceration.

Radical surgery
Operative mortality: There were 4 operative deaths in the 13 patients who underwent pancreacticoduodenectomy. In 1 patient the cause of death was not recorded but her condition remained poor throughout the postoperative period and she died on the fifth day. Two patients died of haemorrhage; one from operative damage to the portal vein. The other died on the fourth day; at post-mortem examination bleeding was found in association with a necrotic pancreaticojejunostomy. The fourth patient who died collapsed suddenly on the tenth postoperative day. At post-mortem he was found to have had a massive pulmonary embolus. All the anastomoses were found to be intact.

The mean age of the patients who died was 65 years compared with 55 years for those who survived the operation. Only 1 patient older than 70 years survived and only 1 patient younger than 65 years died (*Table VIII*).

The mean serum bilirubin level in the patients who died was 18 mg per cent and in those who survived 10 mg per cent. No patient with bilirubin below 10 mg per cent at the time of operation died (*Table VIII*).
Late results: Nine patients survived for longer than 1 month after the operation. Five patients have since died at a mean of 11 months (range 5–18) after operation. It is assumed that all these patients died from recurrence although histological proof was not always available.

Four patients are still alive and clinically recurrence-free between 12 and 44 months (mean 32) later. If all these patients died now the mean survival following successful operation would be 21 months.

Late complications apart from recurrence have been few. There have been no examples of anastomotic ulcer. One patient has steatorrhoea which is satisfactorily controlled by pancreatic extract. One patient has had a single episode of ascending cholangitis.
Other radical procedures: One patient had a transduodenal excision of an ampullary lesion and died of a myocardial infarct 3½ years later. There was no clinical evidence of recurrent disease although a post-mortem was not held.

One patient had an excision of the tail of the pancreas for carcinoma. She died in the early postoperative phase. Permission for a post-mortem examination was not obtained and the cause of death was not established.

Discussion

This group of patients does not seem to differ significantly from other recently published series (e.g. Grieve, 1973) in respect of the site of the tumour and age. However, the sex ratio is more nearly 1 : 1 than is usually recorded and this does not seem to be related to age or the site of the tumour, as suggested by Wynder et al. (1973).

The occurrence of 15 cases of diabetes mellitus raises the possibility of there being a causal relationship between the two diseases. The usually quoted incidence of diabetes mellitus in the general population is between 1–2 per cent and rising with age (Sonksen, 1972). However, Butterfield (1964) suggested that the prevalence is 12–14 per cent, although his criteria for diagnosis depended on the response to a heavy glucose load. Wynder et al. (1973) have shown a significant correlation between diabetes mellitus and pancreatic carcinoma in females but not in males. Other evidence from the present series in favour of at least a casual relationship is the close temporal relationship in the onset of the two diseases and the observation that longstanding diabetics have become unstable shortly before other symptoms have occurred. Walker (1970) reports a case of an abnormal glucose tolerance test reverting to normal after successful pancreaticoduodenectomy. Baron and Nabarro (1973) found 2 cases of carcinoma out of 14 cases of maturity-onset diabetes after subjecting them to extensive investigations. It would seem wise to consider a change in diabetic status as a possible warning of pancreatic carcinoma.

The 14 per cent of patients with gallstone disease probably reflects the prevalence in the community rather than a real association (Rains, 1964). The main interest in this group is the diagnostic problem; it is worth noting that 3 patients had had common duct stones removed at previous laparotomy and, not surprisingly, their subsequent obstructive jaundice had been attributed to recurrent calculi. In view of the possible association between ulcerative colitis and carcinoma of the biliary tract (Ross and Braasch, 1973), it is interesting to note two such instances in the present series.

There is insufficient material to analyse the relative merits of the different procedures used, but in general cholecystoduodenostomy has given satisfactory biliary diversion and has been easy to perform. Subsequent duodenal obstruction does not appear to be associated with a recurrence of jaundice.

Duodenal obstruction has been a significant complication following successful biliary diversion. It is suggested from these results that a gastro-enterostomy should be added to the procedure in all cases. Liver deposits need not be a contra-indication because some of these patients survive 6 months or more. The addition of this procedure adds to the operating time but will spare 1 patient in 5 unpleasant and avoidable symptoms, only relieved by a further operation.

The 13 per cent 1-year survival following palliative surgery does not differ greatly from other series (Gill et al., 1970). Although recurrent jaundice has not been a major problem, the useful palliation achieved has been very limited.

The mortality for pancreaticoduodenectomy in this series is 31 per cent, but the deaths mainly occurred in the earlier years of the survey and the only patient to have died in the last 7 operations did so from a pulmonary embolus.

The late results are poor but 4 patients are still alive and well. The impression has been gained that longer and better palliation has been given to those who have died.

The critics of pancreaticoduodenectomy point to the high operative mortality, the low cure rate and prolonged hospitalization (Crile, 1970). In this series some of these criticisms appear to be unfounded. There is no increase in hospital stay for those having radical surgery (*Table IX*). The mean survival time of 21 months compares with 8 months. In addition, 4 patients are alive and well with 2 having survived 3 years and 2 are still alive between 1 and 2 years later. Only 1 patient has survived 2 years following palliative surgery.

Two-stage procedures have not been prominent in this series, but the relation of mortality to the bilirubin levels above 15 mg per cent suggests that this approach might be considered more often.

Despite its many problems, pancreaticoduodenectomy in selected cases still seems the most satisfactory method of treatment at present available. The decision in part depends on the surgeon's personal philosophy. He has to balance a higher operative mortality, the chance of a major operation for mistaken diagnosis and the chance of a curative operation against a short survival with relief of jaundice and the occasional pleasant surprise when the diagnosis proves to be wrong.

Table IX: COMPARISON OF PALLIATIVE AND RADICAL SURGERY

Surgery	Operative mortality (%)	Mean postoperative survival (mth)	Days in hospital
Radical	31	20	20
Palliative	23	5	25

In Wales there are about 250 cases of pancreatic carcinoma annually (Registrar General, 1971). If the figures in this series are representative, each consultant may be faced by a technically operable lesion once in every 18 months.

Four main conclusions may be drawn from this series:

1. Maturity-onset diabetes should alert the clinician to the possibility of an underlying carcinoma.
2. Pancreaticoduodenectomy was performed in about 15 per cent of cases and appears a worthwhile procedure.
3. Painless jaundice is associated with a higher resection rate.
4. Palliative procedures should include a gastro-enterostomy in addition to a biliary diversion.

Acknowledgement

I should like to thank Mr H. G. Roberts for his permission to study his patients and for his help and encouragement.

References

BARON J. H. and NABARRO J. D. W. (1973) Pancreatic exocrine function in maturity onset diabetes. *Br. Med. J.* **4**, 25–27.

BUTTERFIELD W. J. H. (1964) Summary of results of the Bedford mellitus diabetes survery. *Proc. R. Soc. Med.* **57**, 196–200.

CRILE G. jun. (1970) The advantages of bypass operations over medical pancreatico-duodenectomy in the treatment of pancreatic carcinoma. *Surg. Gynecol. Obstet.* **130**, 1049–1053.

GILL W., CARTER D. C. and DURIE B. (1970) Retroperitoneal tumours. A review of 134 cases. *J. R. Coll. Surg. Edinb.* **15**, 213–221.

GRIEVE D. C. (1973) Adenocarcinoma of the pancreas. A review of 100 cases. *J. R. Coll. Surg. Edinb.* **18**, 221–226.

KRAIN L. S. (1970) The rising incidence of carcinoma of the pancreas. An epidemiological appraisal. *Am. J. Gastroenterol.* **54**, 500–507.

RAINS A. J. H. (1964) *Gallstones: Causes and Treatment.* London, Heinemann, p. 21.

REGISTRAR GENERAL (1971) *Registrar General's Statistical Review of England and Wales for the Year 1971.* London, HMSO, p. 127.

ROSS A. P. and BRASCH J. W. (1973) Ulcerative colitis and carcinoma of the proximal bile ducts. *Gut* **14**, 94–97.

SONKSEN P. H. (1972) Aetiology and epidemiology of diabetes. *Br. J. Hosp. Med.* **7**, 151–156.

WALKER R. J. (1970) The diagnosis of carcinoma of the pancreas. *J. R. Coll. Surg. Edinb.* **15**, 185–190.

WYNDER E. L., MABUCHI K., MARUCHI N. and FORTNER J. G. (1973) A case control study of cancer of the pancreas. *Cancer* **31**, 641–648.

Br. J. Surg. Vol. 62 (1975) 135–140

A comparison of one layer and two layer techniques for colorectal anastomosis

W. G. EVERETT*

SUMMARY

In a randomized prospective clinical trial one layer and two layer techniques have been compared in 92 patients undergoing colorectal anastomosis. The results were assessed radiologically by barium studies on the tenth postoperative day. There was no significant difference in the incidence of anastomotic breakdown with either technique when the anastomosis was performed above the pelvic peritoneal reflection. When the anastomosis was situated below the pelvic peritoneum the incidence of dehiscence was significantly greater when a two layer technique was used.

BREAKDOWN of the anastomosis is still the most significant complication of surgery of the large bowel and accounts for more deaths than any other single cause. The incidence of this complication is highest for colorectal anastomosis, especially when this is performed below the pelvic peritoneal reflection.

There is still doubt concerning the safest method of anastomosis. End-to-end anastomosis, performed in two layers with inversion of the bowel edges, has become the generally recommended technique (Goligher, 1967; Muir, 1969; Turnbull and Kyle, 1969). Nevertheless, some surgeons have found that a single layer anastomosis gives equally satisfactory results (Gambee et al., 1956; Beling, 1957; Trimpi and Kratzer, 1959). Experimental studies have been conflicting (Letwin et al., 1967; Loeb, 1967) and experiments in animals are not always applicable to the situation in man. Recently, Irvin et al. (1973) published the results of a clinical trial of single layer and two layer anastomoses. Their study included patients in whom many different types of operation were performed, involving anastomosis of both the large and small bowel.

It is considered that further data are necessary on this subject and the results of an additional controlled trial in patients undergoing colorectal anastomosis are reported.

Materials and methods

Ninety-two patients undergoing elective resection of the large bowel and end-to-end colorectal anastomosis were studied (*Table I*).

Table I: PRESENT SERIES

Technique	Anastomosis High	Anastomosis Low
One layer	29	11
Two layer	38	14
Total	67	25

The patients were admitted to hospital 48 hours before operation and given a low residue diet. The bowel was prepared by soap and water enemas on the 2 days prior to surgery. A rectal washout was performed on the day of operation and repeated, if necessary, until the washings were clean. No form of antibiotic bowel preparation was used.

All the patients were operated on by the author. The decision to include a patient in the series or not was made only after the bowel had been resected and when it had been ascertained that an intra-abdominal anastomosis could be performed by either technique. Eight patients were excluded and do not form part of the series; in 5 a colo-anal anastomosis was performed; in 3 it was considered that it was only possible to perform a single layer intra-abdominal anastomosis so low in the pelvis. When the decision to include a patient in the series had been made the type of anastomosis to be employed was chosen by a method of random selection.

The single layer anastomoses were performed with interrupted stitches of 4/0 Supramid, passing through all coats of the bowel wall. Nine sutures were used for the back layer and all the stitches were inserted before the proximal bowel was brought down into the pelvis. The back layer stitches were tied with the knots on the inside of the bowel. Gambee-type sutures (Gambee et al., 1956), inverting the mucosa, were used for the front layer.

The two layer anastomoses were constructed with continuous 2/0 chromic catgut for the all-coats stitch, and interrupted Lembert sutures of 4/0 Supramid for the seromuscular layer. The seromuscular stitches of the back layer were inserted first, in a manner similar to that already described for the one layer technique. The inner layer was then sutured with continuous catgut and the front of the anastomosis completed with interrupted Lembert sutures of Supramid. The suture line was marked with two Cushing's clips to aid in its location during subsequent barium examination. In all cases a silicone drain was placed down to, but not in contact with, the anastomosis and allowed to drain freely into a Urebag. The drain was removed on the seventh postoperative day.

In each case the level of the anastomosis was recorded according to its position in relation to the pelvic peritoneum. If situated above or at the level of the peritoneal reflection it was classed as a 'high'

---

* Consultant Surgeon, Addenbrooke's Hospital, Cambridge.

Table II: COMPARISON OF FACTORS WHICH MAY BE RELEVANT TO ANASTOMOTIC DEHISCENCE IN HIGH ANASTOMOSES

	Technique			
	One layer		Two layer	
Average age (yr)	63·2		62·9	
Male: female ratio	1: 1·2		1: 1·3	
	No.	%	No.	%
Pathology				
Carcinoma	19	65	15	39
Diverticular disease	8	28	19	50
Polyps	2	7	4	11
Colostomy				
Preoperative	5	17	6	16
Postoperative	4	14	5	13
Faecal loading	13	45	14	37
Faecal soiling	13	44	12	32

Table III: COMPARISON OF FACTORS WHICH MAY BE RELEVANT TO ANASTOMOTIC DEHISCENCE IN LOW ANASTOMOSES

	Technique			
	One layer		Two layer	
Average age (yr)	66·2		61·4	
Male: female ratio	1: 1·7		1·3: 1	
	No.	%	No.	%
Pathology		82		
Carcinoma		9	13	93
Diverticular disease	1	18	—	7
Rectal polyps	1		—	
Polyps	—		1	
Colostomy				
Preoperative	1	9	0	0
Postoperative	10	91	14	100
Faecal loading	6	54	7	50
Faecal soiling	4	36	4	28

Table IV: INCIDENCE OF ANASTOMOTIC DEHISCENCE

	High anastomoses		Low anastomoses	
	One layer	Two layer	One layer	Two layer
No. of cases	29	38	11	14
Clinical evidence of dehiscence	1*	1†	1†	1‡
Satisfactory anastomosis on barium enema examination	26	38	11	13
Radiological evidence of dehiscence	4 (15·4%)	6 (15·8%)	1 (9·1%)	6 (46·15%)
Total incidence	5 (17·2%)	6 (15·8%)	1 (9·1%)	7 (50%)

* Confirmed by laparotomy.
† Confirmed by barium enema.
‡ Confirmed by post-mortem.

colorectal anastomosis, even though in many instances the rectum was mobilized posteriorly to facilitate fashioning of the anastomosis. When performed below the peritoneal reflection it was termed a 'low' colorectal anastomosis. A covering right transverse colostomy was performed in all but one case of low anastomosis. The amount of faecal loading of the bowel and the degree of contamination occurring during the operation were recorded.

In the postoperative period all cases were given 0·5 g streptomycin 12-hourly and 1 million units of penicillin 6-hourly for 4 days.

The results were assessed by a clinical evaluation, and a limited barium enema examination was performed on the tenth postoperative day to assess the integrity of the anastomosis. Sigmoidoscopy and digital examination of the suture line were avoided.

Results

It is well recognized that the incidence of dehiscence is much greater for low than for high colorectal anastomoses (Goligher et al., 1970). The results have therefore been assessed according to the site of the anastomosis, and are described as 'high' or 'low' according to whether the suture line was above or below the pelvic peritoneal reflection.

Comparability of the groups

Factors which may be relevant to anastomotic dehiscence are age, sex, pathology, faecal soiling, faecal loading of the bowel and the presence or absence of a colostomy before or after surgery. The details of the two groups in which a one layer or two layer technique of anastomosis was used are shown in *Table II* for high anastomoses and in *Table III* for low anastomoses.

Table II shows that the two groups are well matched in all respects except for the pathology. There were more cases of carcinoma in the one layer group and more cases of diverticular disease in the two layer group.

In the low anastomoses (*Table III*) there were differences with respect to age and sex between the two groups which will be referred to later.

Incidence of dehiscence of the anastomosis

Anastomotic dehiscence was detected by clinical and radiological assessment. The results are shown in *Table IV*.

In 4 cases leakage of the anastomosis was suspected on clinical evidence or found at post-mortem. There was 1 death in the immediate postoperative period from ischaemic heart disease, and post-mortem examination revealed a partial breakdown of the suture line. One patient developed peritonitis, and a complete breakdown of the anastomosis was found on re-exploration. In 2 patients anastomotic dehiscence was suspected; one because of pain, and the other on account of a purulent discharge from the drain to the anastomosis. Leakage was confirmed in both cases by barium studies.

Of the 92 patients, barium studies were performed in 90; X-rays were not performed on the 2 patients who came to laparotomy or post-mortem. Of the 90 barium examinations, 2 were unsatisfactory in showing the anastomosis; one because of apparent, but temporary, obstruction at the suture line, and the other because of faeces in the bowel.

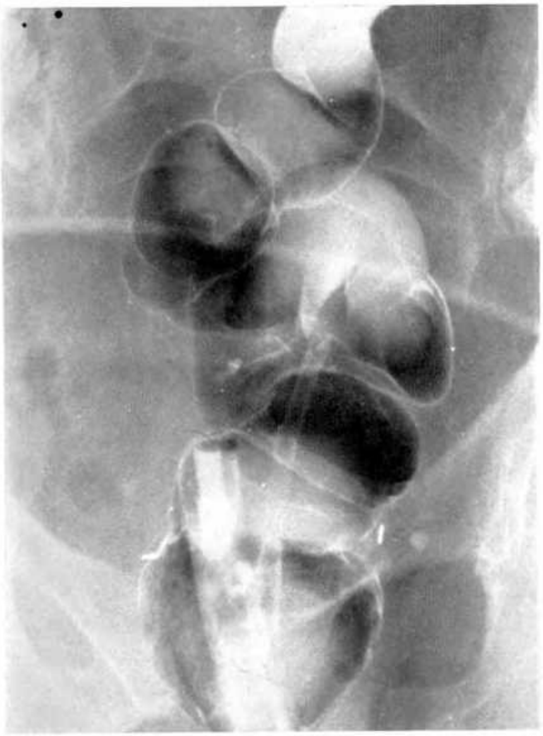


Fig. 1. Low anastomosis, one layer technique.

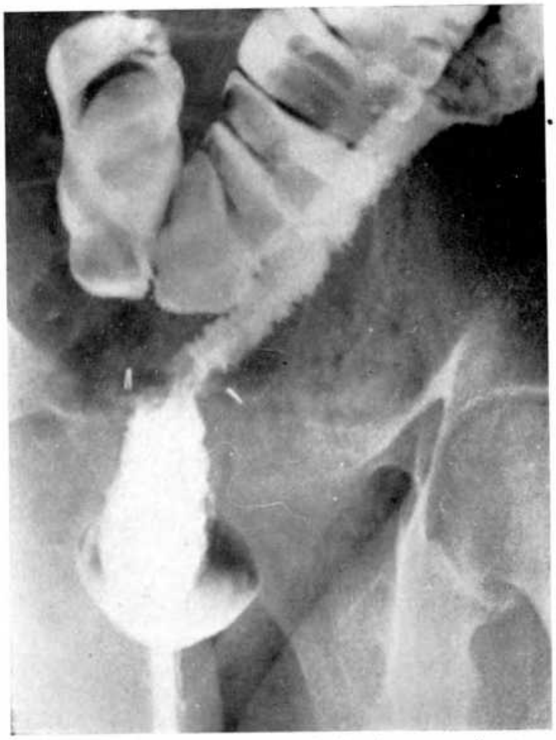


Fig. 3. High two layer anastomosis showing narrowing at the suture line caused by the inturned flange.

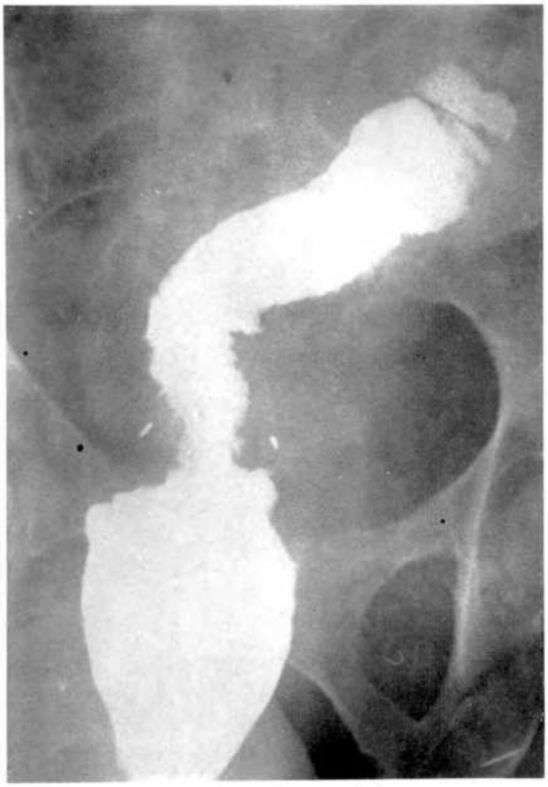


Fig. 2. Low anastomosis, two layer technique.

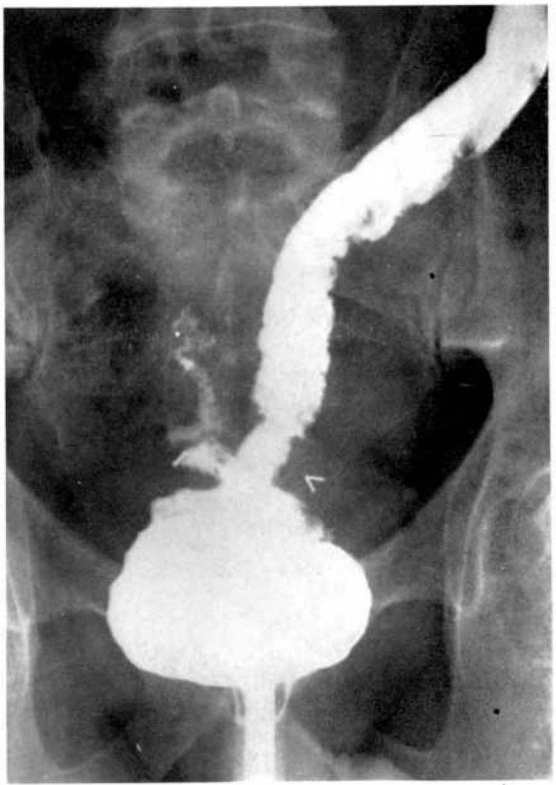


Fig. 4. Low two layer anastomosis showing leakage of average extent.

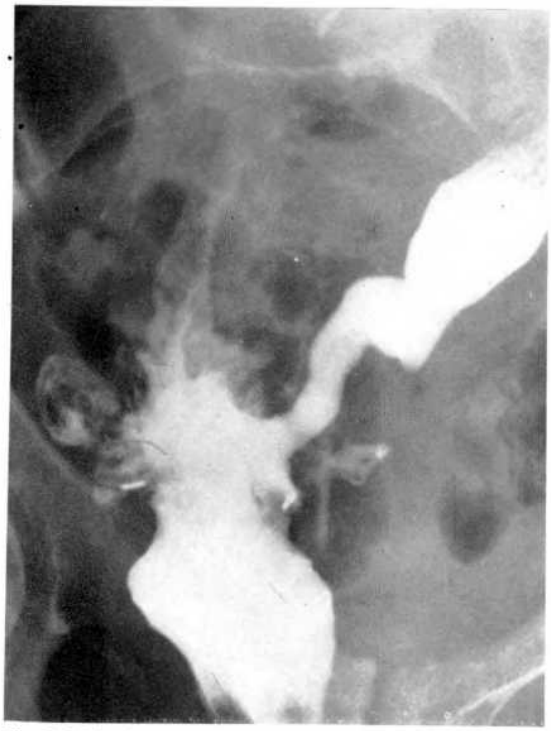


Fig. 5. Major leakage occurring in a low anastomosis (with covering colostomy) with no symptoms or signs.

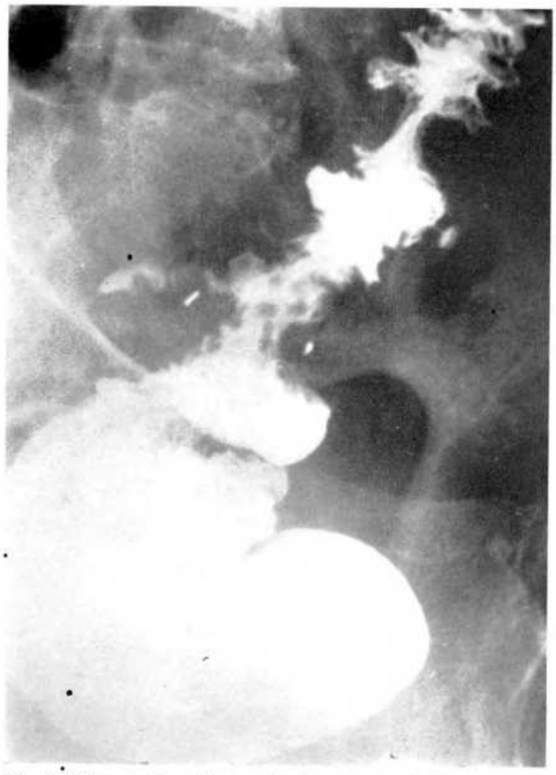


Fig. 6. Minor leakage from a high anastomosis diagnosed clinically.

When assessed radiologically there was no significant difference between the one layer and two layer techniques for high anastomoses ($\chi^2 = 0{\cdot}003$). For low anastomoses a two layer technique was associated with a significantly greater incidence of leakage ($\chi^2 = 3{\cdot}956$, $P < 0{\cdot}05$).

The total dehiscence rate for each group was assessed from the radiological and clinical evidence of anastomotic breakdown. No difference was found between the two groups where a high anastomosis had been performed ($\chi^2 = 0{\cdot}019$). The incidence of breakdown was significantly greater in patients with a low anastomosis in whom a two layer as opposed to a one layer technique had been used ($\chi^2 = 4{\cdot}73$, $P < 0{\cdot}05$).

Dissimilarities in the groups

In the high anastomoses there was a dissimilarity of pathology, particularly with regard to the number of cases of carcinoma and diverticular disease, in each group (*Table II*). In the random allocation there was a significantly greater number of patients with carcinoma who had a one layer anastomosis ($\chi^2 = 4{\cdot}2$, $P < 0{\cdot}05$) and this could be considered prejudicial. However, no significant difference was found when the leakage rate was compared in patients operated on for carcinoma with those having diverticular disease ($\chi^2 = 0{\cdot}004$). It is therefore concluded that there is no difference in the results of using a one layer or a two layer technique for anastomoses above the pelvic peritoneum.

In the patients who had low anastomoses there were dissimilarities of age and sex in the two groups. A younger average age was found in the two layer group, but this gave a favourable bias to the group which did worst. There were considerably more men than women in the two layer group. It could be argued that it is technically more difficult to perform a low anastomosis in a man and this might explain the higher leakage rate in this group. The converse was true for the one layer group. Statistical analysis failed, however, to show a significant difference in the distribution of men and women in the one layer and two layer groups ($\chi^2 = 1{\cdot}062$). The leakage rate was not influenced by sex in the two layer group ($\chi^2 = 0{\cdot}112$), or in the total series of low anastomoses ($\chi^2 = 0{\cdot}98$).

Radiological appearance of anastomoses

The site of anastomosis would have been difficult to locate with accuracy in several cases if it had not been marked with Cushing's clips. In general, the anastomoses performed with the one layer technique (*Fig.* 1) were wider than those in which a two layer technique had been used (*Fig.* 2). In some cases there was quite a marked flange produced by the two layer technique (*Fig.* 3) with apparent narrowing of the bowel lumen. This was not seen with one layer anastomoses. The slight narrowing of the two layer anastomoses did not appear to be of any importance. In one patient who had a one layer anastomosis there was obstruction of the flow of barium at the suture line and the examination was therefore abandoned. There was, however, no clinical evidence of obstruction in this case or in any other patient. Late obstructive symptoms developed in one patient who had a high two layer anastomosis. A barium enema on the tenth postoperative day showed a wide anastomosis with a small leak. Subsequent X-rays demonstrated a fibrous stricture at the suture line which was later resected.

The majority of radiological leaks were of a fairly minor degree and their extent was, in most cases, similar to that shown in *Fig*. 4.

There was no correlation between the extent of the leakage, as assessed radiologically, and the clinical picture. In some cases very large leaks occurred without pain, elevation of temperature or drainage of pus or faecal fluid from the drain site (*Fig*. 5). The minor anastomotic leak shown in *Fig*. 6 was, however, diagnosed by the presence of pain, pyrexia and abdominal tenderness.

Discussion

Dehiscence of the anastomosis is the most significant complication of colorectal anastomosis. It accounts for more deaths than any other single cause (Everett, 1970). The incidence of dehiscence following low colorectal anastomosis was found by Goligher et al. (1970) to be almost 70 per cent, when this was assessed by digital palpation, sigmoidoscopy and barium examination. For this reason it is generally felt that low restorative resections must be accompanied by a protecting transverse colostomy.

The safest method of performing an anastomosis has been a matter of dispute. Most surgeons recommend an inverting technique using two layers of sutures (Goligher, 1967; Muir, 1969; Turnbull and Kyle, 1969), but for many years others have advocated anastomosis with a single layer of sutures (Maunsell, 1892; Gambee et al., 1956; Beling, 1957; Trimpi and Kratzer, 1959). In a retrospective study of 437 anastomoses Buchin and Van Geertruyden (1960) concluded that there was a lower incidence of dehiscence with a single layer technique. A prospective clinical trial of single layer and two layer anastomoses has recently been performed by Irvin et al. (1973). Several different types of anastomosis were performed including ileoileal, ileocolic, ileorectal, colorectal and colocolic. There were no low colorectal anastomoses in the series. The incidence of dehiscence in the single layer group was 17 per cent, and 16 per cent in the two layer group. The conclusion was that there was no advantage in either one of these methods over the other.

In the present study no significant difference was found between one layer and two layer techniques when the anastomosis was performed above the pelvic peritoneal reflection. The incidence of dehiscence (15 per cent) was very similar to that of Irvin et al. (1973). The leakage rate was considerably greater when a two layer technique was used for low colorectal anastomosis. There are two possible explanations for this:

1. The blood supply to the rectal stump might be rendered precarious through mobilization and ligation of the middle rectal arteries. In these circumstances a double layer of stitches could cause ischaemia of the suture line where a single layer might not. In practice, there is usually brisk bleeding from the rectal stump and its blood supply appears to be as good as that of the colon to which it is being joined.

2. As pointed out by Halsted (1887), there is only one layer of the bowel wall which has any substantial strength and this is the submucosa. The muscle layer of the rectal stump holds stitches poorly, perhaps because of the absence of a serosal layer. It is therefore even more important in anastomosis of the rectum that every stitch should pick up the submucosa. With a one layer through-and-through stitch the submucosa is included with certainty in every bite. When a two layer anastomosis is performed low in the pelvis, placing the stitches accurately is not easy and it is especially difficult to ensure that the submucosa is included in the Lembert stitches. This applies particularly to the back layer of the anastomosis, and it is perhaps significant that, in the experience of the author, this is the common site of leakage from the suture line.

It is undoubtedly true that it is much easier to perform an anastomosis in the pelvis with one layer of stitches than with two, and when the suture line is extremely low an anastomosis can sometimes only be achieved by a one layer technique.

In the experience of the author, a one layer technique gives better results than a two layer method for low colorectal anastomosis, and the accuracy with which the sutures are placed seems to be of particular importance.

Acknowledgements

I am indebted to Dr F. R. Berridge and his colleagues of the Radiology Department, Addenbrooke's Hospital, Cambridge, for performing the radiological studies, Mr F. H. J. Beard of the Department of Medical Photography for the illustrations and Mr D. Sampson for help with the statistical analysis.

References

BELING C. A. (1957) Single layer end to end intestinal anastomosis. *Am. J. Gastroenterol.* **27**, 374–378.

BUCHIN R. and VAN GEERTRUYDEN J. (1960) Valeur comparée des sutures intestinales en un plan et en deux plans. Etude expérimentale et clinique. *Acta Chir. Belg.* **59**, 461–480.

EVERETT W. G. (1970) Colonic anastomosis. MCh Thesis, Oxford.

GAMBEE L. P., GARNJOBST W. and HARDWICK C. E. (1956) Ten years' experience with a single layer anastomosis in colonic surgery. *Am. J. Surg.* **92**, 222–225.

GOLIGHER J. C. (1967) *Surgery of the Anus, Rectum and Colon.* London, Baillière, Tindall & Cassell, pp. 533–535.

GOLIGHER J. C., GRAHAM N. G. and DE DOMBAL F. T. (1970) Anastomotic dehiscence after anterior resection of rectum and sigmoid. *Br. J. Surg.* **57**, 109–118.

HALSTED W. S. (1887) Circular suture of the intestine —an experimental study. *Am. J. Med. Sci.* **94**, 436–461.

IRVIN T. T., GOLIGHER J. C. and JOHNSTON D. (1973) A randomized prospective clinical trial of single-layer and two-layer inverting intestinal anastomoses. *Br. J. Surg.* **60**, 457–460.

LETWIN E., WILLIAMS H. T. G. and HARRISON R. C. (1967) The experimental healing of soft tissues. *J. R. Coll. Surg. Edinb.* **12**, 121–132.

LOEB M. J. (1967) Comparative strength of inverted, everted and end-on intestinal anastomoses. *Surg. Gynecol. Obstet.* **125**, 301–304.

MAUNSELL H. W. (1892) A new method of intestinal surgery. *Am. J. Med. Sci.* **103**, 245–257.

MUIR E. G. (1969) Colectomy. In: ROB C. and SMITH R. (ed.) *Operative Surgery*, Vol. 5. London: Butterworths, p. 658.

TRIMPI H. D. and KRATZER G. L. (1959) Alloy steel wire as suture material for open anastomoses of the large intestine. *J. Am. Geriatr. Soc.* **7**, 153–160.

TURNBULL R. B. and KYLE K. (1969) Operations for cancer of the distal transverse colon and left colon. In: ROB C. and SMITH R. (ed.) *Operative Surgery*, Vol. 5. London: Butterworths, p. 665.

Br. J. Surg. Vol. 62 (1975) 141–143

Complete disappearance of popliteal arterial thromboses in 2 patients

KENNETH BLOOR AND VICTOR COPE*

SUMMARY

Two young male patients with complete spontaneous resolution of popliteal thrombosis are described. The thromboses had been present for roughly 3½ and 4 months. Such resolution has not been previously reported. The cause of the lesions is unexplained. It is suggested, should such a lesion be encountered, that the correct treatment is exploration to exclude adventitial cysts and popliteal entrapment, and simple evacuation of clot and anticoagulation.

TOTAL spontaneous resolution of an arterial thrombosis does not appear to have been previously reported. In the 2 cases to be described, popliteal thrombosis present for 3 months or more resolved completley. In both cases the presence and disappearance of the thrombosis were proved by arteriography.

Case reports

Case 1: J. W., an 18-year-old male, was a keen footballer, and after playing in a match on 15 January 1962 noticed tiredness of his right leg. No injury to the leg was remembered. Thereafter he had gradually increasing pain behind the knee, radiating into his calf on walking. His right foot also went cold and numb on exercise. He was a non-smoker. He was seen in the Vascular Clinic of Manchester Royal Infirmary on 22 February 1962, when pulses were absent at the right ankle and oscillometry demonstrated reduced pulsations below the knee on the right side. Between this attendance and his admission on 3 March his symptoms disappeared, and on admission pulses were present at both ankles and oscillations were equal and good in both legs. There was no clinical evidence of heart disease and the electrocardiogram was normal. Other investigations did not reveal any abnormality. His erythrocyte sedimentation rate, haemoglobin and white cell count were normal. His serum cholesterol was 225 mg/100 ml. On exercise on a walking machine he had no pain at 2½ m.p.h. after half a mile. The speed was increased to 3½ m.p.h. for a further half a mile without pain. He was discharged without treatment.

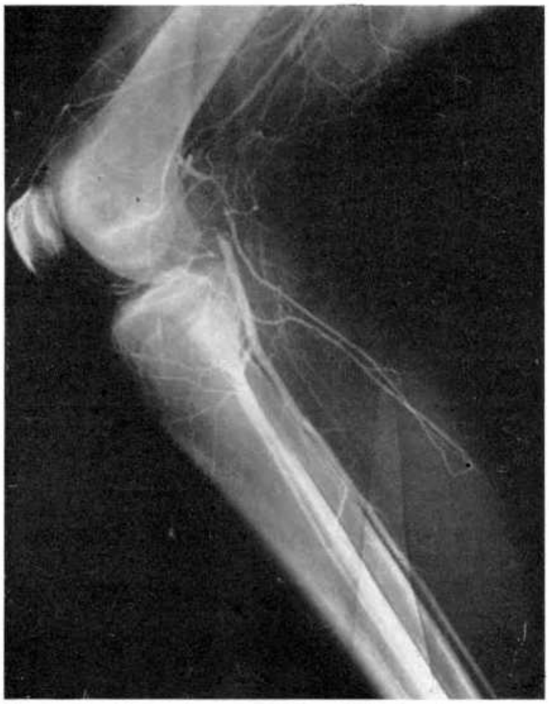


Fig. 1. *Case* 1. Arteriogram, 30 May 1962, showing upper popliteal thrombosis.

For 2 weeks after discharge he had no trouble, but after a game of football the pain in the calf and cold foot on walking recurred, and on readmission on 21 May 1962, pulses were absent and oscillations reduced below the knee in the right leg. A right femoral arteriogram was performed by cutdown on the common femoral artery on 30 May 1962 (*Fig.* 1). This showed a block about 5 cm in length in the upper popliteal artery. There was no recanalization, and there was a good collateral circulation. On walking at 2½ m.p.h. pain occurred after 700 yards and he was halted at 1100 yards after the speed had been increased to 4 m.p.h. In view of the mild nature of his claudication no treatment was offered. Shortly after discharge from hospital his claudication disappeared again. A further arteriogram was performed on 28 September 1962 (*Fig.* 2). This demonstrated patency of the popliteal artery, which appeared normal apart from a slight irregularity and a small filling defect immediately above the femoral condyles. Thus, on the second occasion his thrombosis was present for more than 2 months. He was discharged without treatment.

He was seen again on 12 May 1966 for an unrelated complaint. He had had no recurrence of intermittent claudication since 1962 and his right ankle pulses were present. All investigations including an electrocardiogram were normal. His serum cholesterol was 240 mg/100 ml. Efforts to trace him since then have unfortunately failed.

Case 2: B. B., a 35-year-old male, worked as a fireman. Both at work and at home whilst doing odd jobs he was in the habit of sitting on his right leg with the knee bent and the lower leg underneath his left thigh. He had a family history of arterial disease in that his father suffered from angina pectoris. The patient was a non-smoker.

His symptoms started suddenly shortly after he had been sitting on his right leg for 2–3 hours whilst working in July 1971. Initially his intermittent claudication was not severe but it gradually worsened until he was only able to walk 30 yards, and by the end of September 1971 he had begun to have typical nocturnal rest pain in his right foot which was relieved by hanging the foot over the side of the bed. He was admitted on 25 October 1971. His blood pressure was within normal limits at 140/90. He had no clinical evidence of arterial disease apart from the absence of pulses at the right ankle. The foot was markedly pale on elevation and there was diminution of sensation to a pin prick. An arteriogram showed a normal arterial tree apart from a short popliteal thrombosis

---

* Manchester Royal Infirmary.

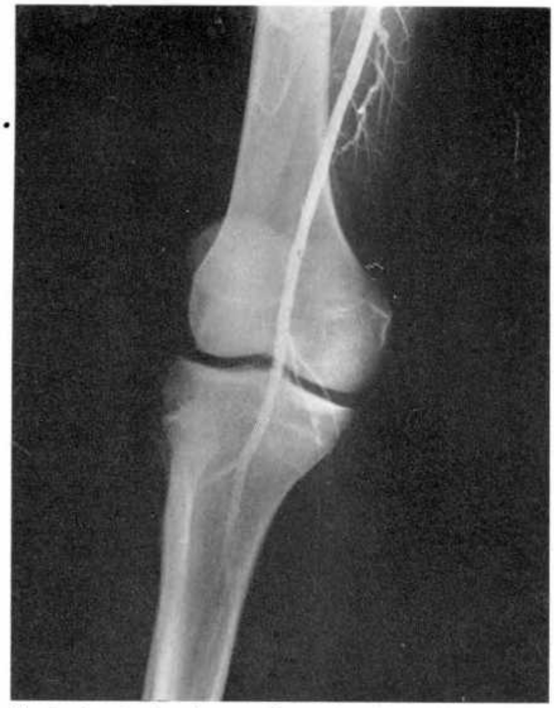


Fig. 2. *Case* 1. Arteriogram, September 1962, showing resolution with a small filling defect at the level of the adductor tubercle.

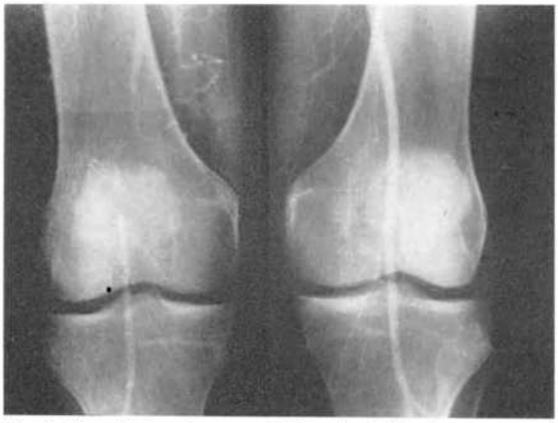


Fig. 3. *Case* 2. Arteriogram, 25 October 1971, showing upper popliteal thrombosis on the right side.

in the right leg about 2 cm in length and about 4 cm above the knee joint (*Fig*. 3).

In view of his youth and the short time since the commencement of his symptoms it was considered that operative treatment should not be undertaken immediately and he was discharged. The patient's rest pain disappeared that evening. His intermittent claudication improved and he was able to walk a mile without pain at review a month later.

He was readmitted in January 1972 for a repeat of the peripheral arteriograms. This showed complete restoration of the arterial lumen (*Figs*. 4, 5) apart from a small filling defect in the artery similar to that seen in the previous patient. On this admission his blood count was within normal limits, the haemoglobin was 14·7 g and the platelet count was 220 000/mm³. Coagulation studies showed no abnormality in the plasma clotting time, the prothrombin time and the plasma fibrinogen, which was 334 mg/100 ml. The fibrinolytic system appeared to be normal in that the euglobin lysis time was 300 minutes and fibrin degradation products were within the normal range. Total serum cholesterol was 200 mg/100 ml and the serum lipoprotein pattern in the fasting state was normal. When seen in the outpatients' department on 17 March 1973, the patient was able to walk indefinitely without pain at a normal pace and all peripheral pulses were present.

He was advised to abandon his habit of sitting with his right leg bent underneath him. No other treatment was prescribed.

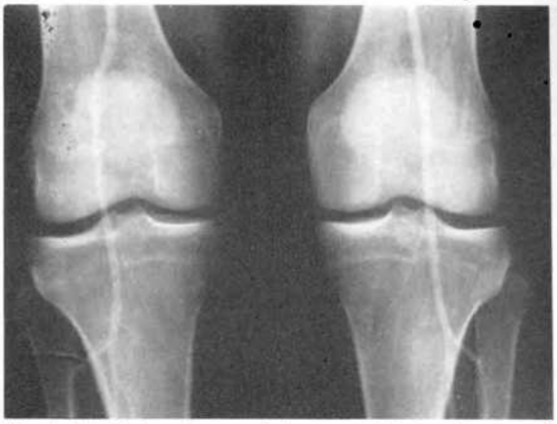


Fig. 4. *Case* 2. Arteriogram, 5 January 1972, showing resolution of the thrombus.

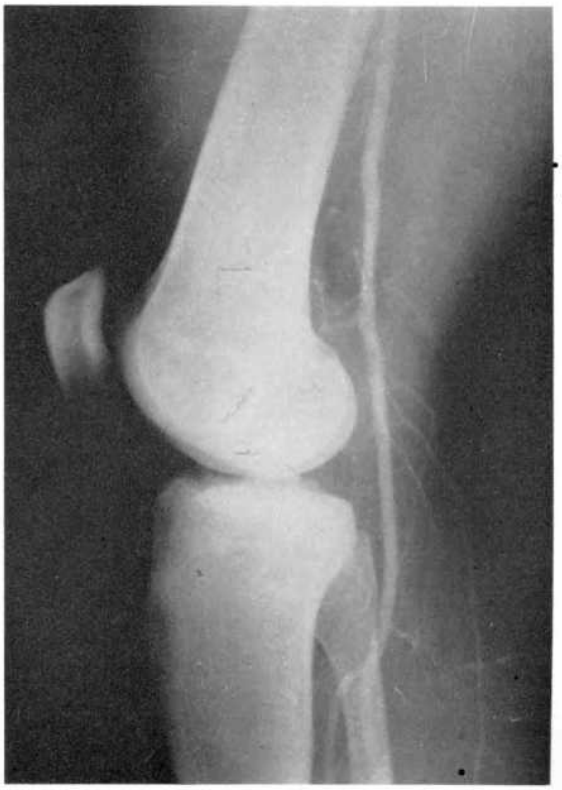


Fig. 5. *Case* 2. Lateral arteriogram, 5 January 1972, showing a small filling defect level with the top of the femoral condyles.

Discussion

Case 1 appears to have had resolution of a popliteal arterial thrombosis on two occasions. Resolution may have been incomplete in the first place but there can be no doubt about its final disappearance. Thus the patient had had partial or complete occlusion for 6 weeks initially, and complete occlusion for more than 2 months. In *Case* 2 the occlusion had been present for 4 months before disappearance. In both cases the thrombosis may be related to indirect damage to the vessel wall; in *Case* 1 both exacerbations were related to playing football and in *Case* 2 the patient attributed it to his curious habit of sitting on his leg. It is, however, difficult to suggest a mechanism for this damage with normal anatomy. Such indirect trauma could only be conceived of in the case of an anatomical abnormality, such as an aberrant muscular or fascial band.

In neither case was there any suggestion of a peripheral or central lesion which could cause emboli. The position of the block in both cases is not in the site in which one would expect an embolus, i.e. it is not impacted at a bifurcation. Complete or partial resolution of an embolus with thrombosis is not uncommon in the first 2 or 3 days. After this time, however, resorption of the clot, for reasons discussed below, is not within anyone's clinical experience.

The popliteal artery is a favoured spot for arterial occlusions and in young people there are two uncommon lesions, namely cystic adventitial disease and the popliteal entrapment syndrome, which may lead to popliteal thrombosis. Cystic adventitial disease produces a fairly sudden onset of intermittent claudication which gradually worsens. There are characteristic changes of arterial narrowing, which may be one-sided or hour-glass-shaped, immediately above the knee joint, and eventually thrombosis may occur (Lewis et al., 1967). There is no recorded case of spontaneous improvement (Haid et al., 1970). Should the associated intravascular thrombus resolve in such a case deformation of the artery would persist and would easily be visible on the post-resolution arteriograms.

The anatomical abnormality in the popliteal entrapment syndrome can be of two types (Insua et al., 1970). In type I the popliteal artery passes medially to the medial head of the gastrocnemius and underneath it. In this type there is an easily observable medial displacement of the artery, which was obviously not present in either of our cases. In type II, however, there is an abnormal fascial band running across the popliteal artery, which is normally placed. This produces a slight deviation of the artery similar, it might be argued, to that seen in *Fig*. 4. On inspection, however, the deviation in *Fig*. 4 is higher than would be expected from such a cause (cf. *Fig*. 3.27 in Eastcott, 1969). Again there is no suggestion in the literature (Insua et al., 1970, and the following discussion) that spontaneous resolution of a thrombosis associated with the popliteal entrapment syndrome has ever occurred.

If thrombosis occurs in a normal artery the organization of the clot is quite rapid. There is proliferation of the endothelium into the clot, followed subsequently by penetration by small arteries and eventually partial recanalization may occur with the development of muscle fibres and a microscopic appearance similar to an artery inside an artery. It is surprising therefore that thromboses present for 3 and 5 months respectively should not be sufficiently organized to prevent lysis. On the other hand, in abnormal arteries lysis of thromboses by streptokinase therapy has been undeniably demonstrated to occur in blocks of up to 12 months' duration, and this happens in a substantial proportion of patients (Martin et al., 1970). One can only presume that the thrombus was not organized and its disappearance was due to the action of natural fibrinolytic activity. Unfortunately *Case* 1 has been lost to follow-up and haematological investigation was not possible. In *Case* 2 no abnormality of coagulation or fibrinolytic activity could be demonstrated, although admittedly investigation was only undertaken some 3 months after the disappearance of the thrombus. In neither case was there any suggestion of an intercurrent illness or of any change in the patient's normal habits which might enhance fibrinolytic activity. The resolution of these thrombi therefore remains a complete mystery.

The condition appears to be extremely rare and no reports have previously appeared in the literature. In any case of popliteal thrombosis in a young man exploration of the popliteal fossa would be thought imperative if symptoms persisted. In such cases cystic adventitial disease or popliteal entrapment would be the most likely finding. Should the thrombosed popliteal artery be exposed, no external lesion found and atheroma appeared to be unlikely, it would be tempting to assume that the condition described here was present and that the only treatment necessary would be arteriotomy and evacuation of the clot followed by anticoagulant therapy with heparin.

References

EASTCOTT H. G. G. (1969) *Arterial Surgery*. London, Pitman.

HAID S. P., CONN J. jun. and BERGAN J. J. (1970) Cystic adventitial disease of the popliteal artery. *Arch. Surg.* **101**, 765–770.

INSUA J. A., YONG J. R. and HUMPHRIES A. W. (1970) Popliteal artery entrapment syndrome. *Arch. Surg.* **101**, 771–775.

LEWIS G. J., DOUGLAS D. M., REID W. and WATT J. K. (1967) Cystic adventitial disease of the popliteal artery. *Br. Med. J.* **3**, 411–414.

MARTIN M., SCHOOP W. and ZEITLER E. (1970) Streptokinase in chronic arterial occlusive disease. *JAMA* **211**, 1169–1173.

Br. J. Surg. Vol. 62 (1975) 144–146

Long term review of the results of rubber band ligation of haemorrhoids

DAVID M. STEINBERG, H. LIEGOIS AND J. ALEXANDER-WILLIAMS*

SUMMARY

A long term assessment (mean 4·8 years) of the value of rubber band ligation treatment for haemorrhoids has been obtained by a questionnaire answered by 125 of 147 patients. Eighty-nine per cent of patients were cured or satisfied with the results of treatment, although complete absence of symptoms was only obtained in 44 per cent. Further conservative treatment (rubber band ligation or manual dilatation) was required in 12 per cent and only 3 (2 per cent) have had a haemorrhoidectomy. Similar results were obtained for patients with the additional symptoms of pain and irritation, the presence of large skin tags and for the majority of third degree piles.

METHODS of treatment of haemorrhoids have been described since antiquity, with writings dealing with various methods of treatment dating back to the Babylonian era (Eastman, 1970). Hippocrates described the use of cautery—a treatment that must have been excruciatingly painful in the pre-anaesthetic era (Holley, 1946). In the twentieth century most treatment has been based on the use of sclerosants (injection) for minor degrees of haemorrhoids, and various methods of excision for prolapsing haemorrhoids (Goligher, 1967).

Much interest recently has been focused on newer conservative methods of treatment in the form of rubber band ligation and manual dilatation (Barron, 1963a; Lord, 1968; Groves et al., 1971). Claims have been made for symptomatic relief with all grades of haemorrhoids, but these have been made without any long term assessment.

A previous report from the Proctology Clinic, The General Hospital, Birmingham (Groves et al., 1971) showed that in a mean follow-up of 18 months, 91 per cent of patients considered that the result of rubber band ligation was excellent or had greatly improved their symptoms.

This paper is based on a subjective assessment by patients of the results of their treatment with rubber band ligation many years before. We believe a subjective or symptomatic assessment to be of more value than objective assessment on proctoscopy. The incidence of haemorrhoids in the general population is as yet unknown, but a study from the Mayo Clinic (Buie, 1960) gave an incidence of 52 per cent in an unselected series of inpatients. In our experience a large number of patients who appear to have haemorrhoids on proctoscopy have no symptoms.

Table I: SYMPTOMS BEFORE RUBBER BAND LIGATION (125 PATIENTS)

Symptom	No. of cases
Bleeding	114
Irritation	48
Pain	54
Prolapse	80
Discharge	29

Mean duration of symptoms before treatment, 4·5 years

Table II: PROCTOSCOPIC EXAMINATION AT INITIAL VISIT 1967–9

		No. of cases
Haemorrhoids:	First degree	6
	Second degree	101
	Third degree	18
Other findings:	Skin tags	53
	Excoriation	8
	Painless fissure	3

Materials and methods

Prospective documentation of symptoms, proctoscopic findings and details of treatment was obtained for 147 patients who were treated by rubber band ligation between 1967 and 1969. All these patients were treated at monthly intervals until cessation of symptoms by the method described by Groves et al. (1971) using a Barron Ligator. In June 1973 a follow-up questionnaire was sent to each of these 147 patients. One hundred and twenty-five patients (81 per cent) have replied. The mean time since completion of their rubber band treatment was 4·8 years with a range of 3·5–6·0 years. The general practitioners of 10 patients have been contacted and it is known that only 2 have had further trouble with occasional mild irritation. The names of the remaining 12 patients lost to follow-up have been submitted to the Birmingham Regional Hospital Board statistics computer and none has been recorded as having had a haemorrhoidectomy in this region at any time since their rubber band ligation.

The analysis of the results will consider only the 125 patients of whom full follow-up details are available. All patients dissatisfied or suffering moderate or severe residual symptoms have been examined at the outpatients' clinic.

The presenting symptoms of the 125 patients are shown in *Table I*, the majority of patients presenting with bleeding and prolapse. 'Pain', usually episodic, was a feature in 44 per cent. Any patient found to have a painful fissure or fistula at the time of initial presentation was excluded from this survey. The mean duration of symptoms before treatment was 4·5 years.

The proctoscopic findings at the initial visit are shown in *Table II*. First degree piles are those remaining within the anal canal; second degree, prolapse

---

* Proctology Clinic, The General Hospital, Birmingham. Requests for reprints to J. Alexander-Williams.

during defaecation but reducing spontaneously; third degree piles, prolapse at any time or requiring digital replacement. During the time over which these patients were treated a few other patients presenting at the clinic with gross third degree piles were subjected to haemorrhoidectomy without any attempt at conservative treatment. However, the incidence of haemorrhoidectomy in the patients referred to the Proctology Clinic over the past 2 years has been less than 4 per cent.

The rubber band ligation was usually performed as one application per session, based on the suggestion of Barron (1963a), that discomfort was minimized if only one at a time was applied. The principle was to continue treatment sessions on a monthly basis until patients were symptom free. The majority of patients required two or three sessions.

Results

In response to the first question on the questionnaire 116 patients (93 per cent) said that they considered the treatment worth while. The second question asked for a more detailed subjective assessment of the treatment. The answers are shown in *Table III.*

In answer to the question: 'What do you think of the result of the treatment?' an excellent or good result was reported by 111 (89 per cent), 12 (10 per cent) said the treatment achieved very little and in only 2 (1 per cent) were the symptoms made worse.

The patients were asked to make an assessment of individual symptoms, including severity and duration. The results are shown in *Table IV.* It was of interest that some patients considered themselves completely cured despite some occasional discomfort or even spotting of blood while others who stated that they were now symptom free classified their result as being much improved but not perfect. The majority of recurrent symptoms were those of intermittent bleeding, prolapse and/or discomfort.

Since completing the course of rubber band ligation 107 patients have received no further active treatment for their haemorrhoids, 8 (6 per cent) have required a further course of rubber band ligation and all but one are now satisfied with a good result. The mean time interval before the second course of ligation was 2 years. Six patients (5 per cent) have been treated with a manual dilatation and one has had a lateral sphincterotomy for persistent symptoms. All have since been cured or greatly improved. Only 3 patients (2 per cent) out of the 147 have required a haemorrhoidectomy.

The results of treatment of patients whose principal presentation of bleeding was complicated by irritation and/or pain were compared with those who had bleeding as a single presentation or associated with prolapse. The results are shown in *Table V.* There was no difference in terms of subjective result, of symptomatic relief or need for further treatment. Similarly 18 patients assessed as having large or third degree piles had similar results to those with intermediate or second degree ones. Patients with large skin tags suffered only slightly less good results than the remainder, with 84 per cent having a good result and 16 per cent being a little better or the same.

Table III: REPLIES TO QUESTIONNAIRE

Question: To 125 patients	Answer
As a result of the treatment are you now:	Yes
Completely cured?	54
Much improved but not perfect?	57
A little better?	9
Same as before treatment?	3
Worse than before treatment?	2

Cured or much improved	111 (89%)
Little or no improvement	12 (10%)
Worse	2 (1%)

Table IV: SYMPTOMS SINCE RUBBER BAND LIGATION

Result:	No. of cases:	
Symptom free		55 (44%)
Symptoms		70 (56%)
Continuous	14	
Intermittent	49	
One episode	7	

Table V: PRESENTING SYMPTOMS COMPARED WITH RESULTS OF TREATMENT

	Presentation			
Subjective assessment	A		B	
Cured	19	91%	34	90%
Greatly improved	13		29	

A, Patients with bleeding as a single presentation or associated with prolapse; 35 patients.
B, Patients with bleeding complicated by irritation and/or pain; 70 patients.

Discussion

Before evaluating the results in this paper it is necessary to appreciate that treatment of the patients' piles has been carried out with the aim of obtaining symptomatic relief, without necessarily removing all haemorrhoidal tissue. Proctoscopic examination of asymptomatic patients after a course of rubber band ligation frequently shows evidence of residual haemorrhoids. Injection therapy, which has a similar objective, seems to show good results for first degree and smaller second degree piles. However, it is generally believed that injection produces poor results in patients with large haemorrhoids, and with all degrees of piles it is subject to a high symptomatic recurrence rate (Millegan, 1939; Barron, 1963b). Haemorrhoidectomy, which aims to excise most of the haemorrhoidal plexus of veins should produce lasting results. In a follow-up of 138 patients reviewed at 5 years after haemorrhoidectomy only 5 per cent had recurrent symptoms of pain, prolapse or bleeding, but 26 per cent complained of minor degrees of anal incontinence (Bennett et al., 1963). Despite the freedom from recurrent symptoms of piles haemorrhoidectomy is often a painful procedure; it involves the patient being in hospital for from 5 to 10 days with an additional time off work of 2–6 weeks; furthermore, it is not without complications such as secondary haemorrhage, stenosis or incontinence (Goligher, 1967).

The present survey shows that after rubber band ligation the majority (89 per cent) of patients considered themselves cured or greatly improved by the treatment. However, only 44 per cent were completely symptom free. Intermittent mild discomfort, occasional spotting of blood and an awareness of lumps at the anus were the principal residual symptoms. Nevertheless, many patients expressed themselves as extremely happy with this situation compared with their state before treatment.

Patients who suffer persistent or severe recurrent symptoms after rubber band ligation can be treated by further conservative measures; 15 patients (12 per cent) had either a further rubber band ligation, an anal dilatation or a lateral sphincterotomy. Only one patient required a haemorrhoidectomy due to failure of the technique to control symptoms. Two others have had a haemorrhoidectomy at their own request when symptoms later recurred.

The early symptomatic relief previously reported by us (Groves et al., 1971) and now the longer follow-up reported here have encouraged us to pursue a policy of treating third degree haemorrhoids by rubber band ligation, particularly in the elderly and patients whose general condition contraindicates haemorrhoidectomy. Similar experience in treating the majority of patients with haemorrhoids by this outpatient procedure is reported from the Lahey Clinic (Corman and Verdenhamer, 1973).

Rubber band ligation is a moderately effective method of treating symptoms due to haemorrhoids, with undoubted economic advantages over a conventional haemorrhoidectomy. We feel it has logistic and administrative advantages over the common conservative management, manual dilatation.

One of us (H. L.), a general practitioner who is a clinical assistant in the Proctology Clinic, has also performed 200 rubber band ligations in his group practice. It is our belief that this method of conservative management can be learnt by general practitioners and practised successfully without having to refer patients to hospital clinics. It is, of course, essential that these general practitioners should also learn to examine patients by sigmoidoscopy (to at least 15 cm from the anus) to ensure that they do not fail to detect coincident or underlying tumour or proctitis.

Acknowledgements
D. M. Steinberg is a Raine Travelling Scholar, University of Western Australia. H. Liegois is supported by a grant from the British Medical Association.

References

BARRON J. (1963a) Office ligation of internal hemorrhoids. *Am. J. Surg.* **105**, 563–570.

BARRON J. (1963b) Office ligation treatment of hemorrhoids. *Dis. Colon Rectum* **6**, 109–113.

BENNETT R. C., FRIEDMAN M. H. W. and GOLIGHER J. C. (1963) Late results of haemorrhoidectomy by ligation and excision. *Br. Med. J.* **2**, 216–219.

BUIE L. A. (1960) *Practical Proctology*, 2nd ed. Springfield, Ill., Thomas, p. 737.

CORMAN M. D. and VERDENHAMER M. C. (1973) Hemorrhoidectomy. *Surg. Clins North Am.* **53**, 417–422.

EASTMAN, P. E. (1970) *Outpatient Hemorrhoidectomy Ligation Technique*. New York Medical Examination Publishing Co., p. 13.

GOLIGHER J. C. (1967) *Surgery of the Anus, Rectum and Colon*, 2nd ed. London, Baillière, Tindall & Cassell, ch. 4, p. 155.

GROVES A. R., EVANS J. C. W. and ALEXANDER-WILLIAMS J. (1971) Management of internal haemorrhoids by rubber band ligation. *Br. J. Surg.* **58**, 923–924.

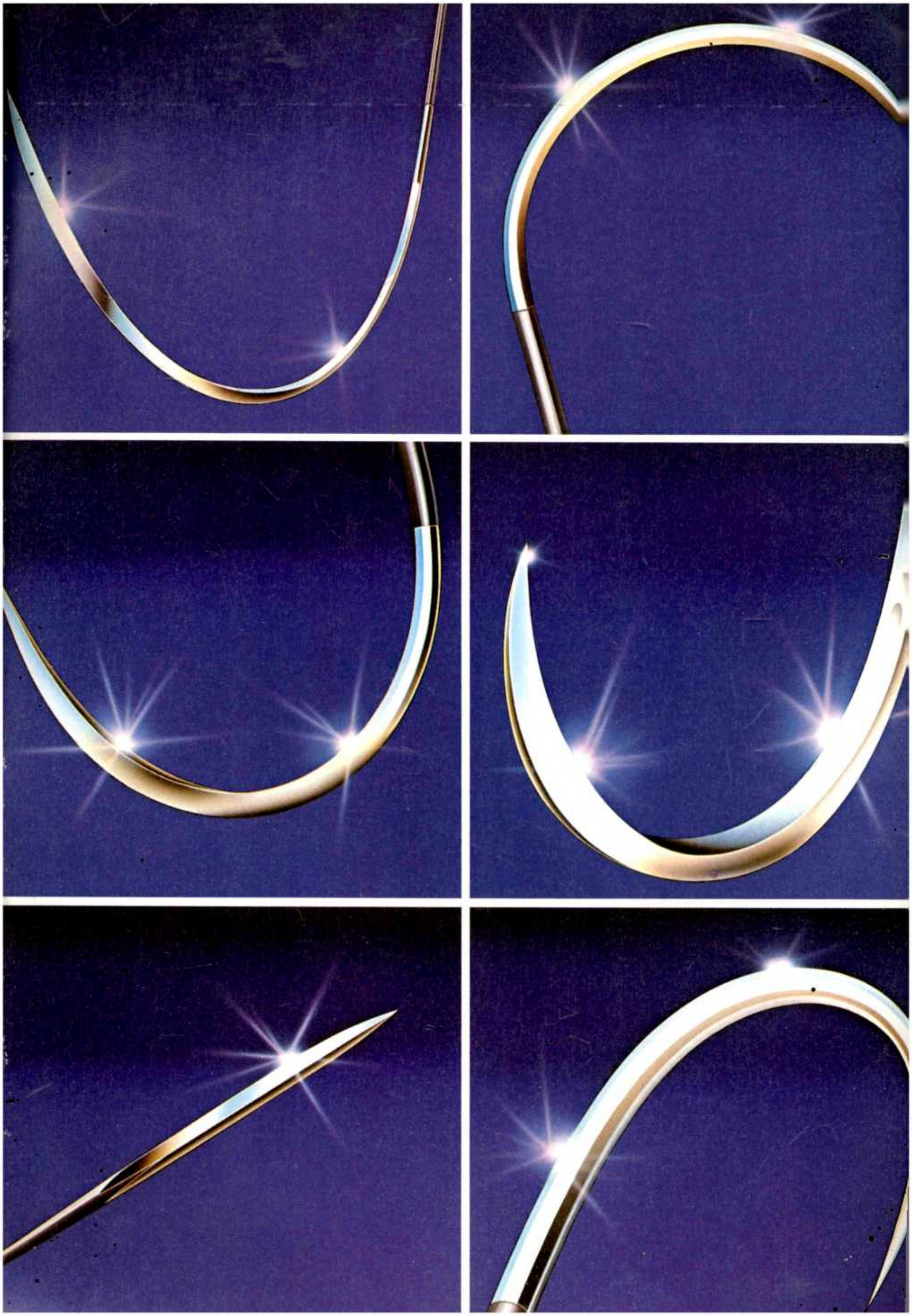
HOLLEY C. T. (1946) History of hemorrhoidal surgery. *South. Med. J.* **39**, 536–541.

LORD P. (1968) A new régime for the treatment of haemorrhoids. *Proc. R. Soc. Med.* **61**, 935–936.

MILLEGAN E. T. C. (1939) Haemorrhoids. *Br. Med. J.* **2**, 412.

the range is ours
the choice is yours

ETHICON
TRADEMARK
Eyeless needled sutures



WE MAKE SOME VERY IMPORTANT POINTS

ETHICON* Eyeless Needled Sutures offer three outstanding advantages over traditional eyed needles.

Point 1 A new sharp needle every time.

Point 2 Reduced trauma–with ETHICON eyeless needles there is no large eye and only one strand of material to pass through tissue.

Point 3 Consistent high quality–by precisely controlled manufacture of a complete sterile suture in a single package.

The choice is yours

Most surgeons agree that there is no universal suture. Most probably there never will be. Each patient, each procedure, and each layer of tissue differs from the next. This is why we at ETHICON manufacture such a comprehensive range of eyeless needled sutures.

You can choose from our wide selection of materials, absorbable and non-absorbable, securely attached to a stainless steel needle of your choice. The consistent high quality of ETHICON eyeless needled sutures provides predictable performance. This enables you to concentrate on the most critical aspect of your surgery–the well-being of the patient.

Reduce Trauma

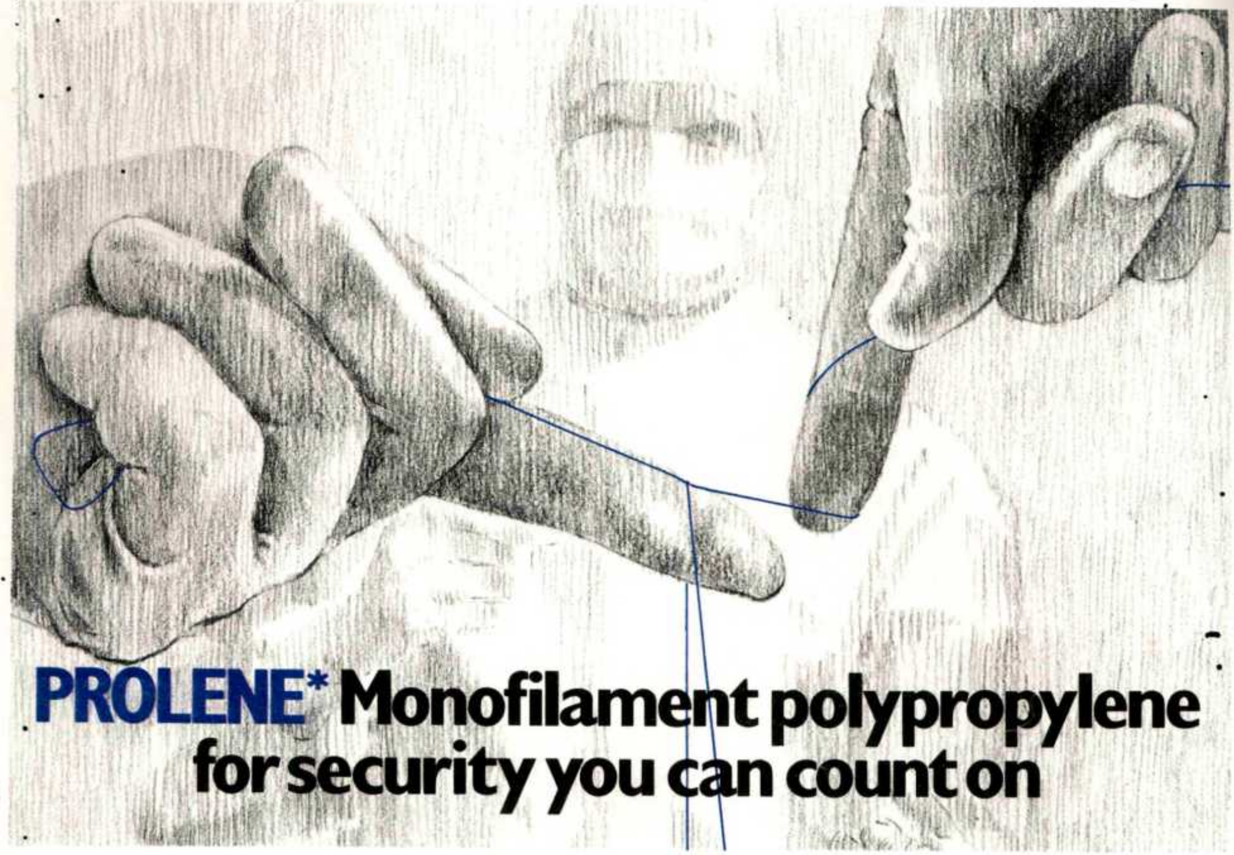
Quality and Reliability at every stage

© ETHICON LTD 1974* Trade Mark

ETHICON
Eyeless needled sutures

Widest range. Finest quality

ETHICON Ltd., Bankhead Avenue, Edinburgh EH11 4HE, Scotland



PROLENE* Monofilament polypropylene for security you can count on

When the reliability of a non-absorbable is required in a contaminated or potentially contaminated field many surgeons are now choosing PROLENE suture. Made from polypropylene, a material of relative biological inertness, monofilament PROLENE suture is not degraded by tissue enzymes and is virtually unaffected by the presence of infection.

Security for extended approximation

Where wound healing may be delayed PROLENE suture can be relied on to retain its tensile strength.

Secure knot-holding

PROLENE suture is able to deform and flatten on knotting to give knot security superior to any other monofilament.

Security through reduced risk of suture extrusion and sinus formation

The specially smooth monofilament structure of PROLENE suture and its ability to tolerate infection extremely well can lessen the risk present with a braided suture in a contaminated wound.

Indications: PROLENE Polypropylene suture may be used wherever a non-absorbable surgical suture is recommended.

Precautions: Unused PROLENE sutures may not be autoclaved more than three times by the standard autoclaving method without loss of strength. Care should be taken to avoid damaging the surface of the material with surgical instruments.

ETHICON

Widest range. Finest quality

© ETHICON LTD 1974* Trade Mark

ETHICON LTD. Bankhead Avenue, Edinburgh EH11 4HE, Scotland.

Br. J. Surg. Vol. 62 (1975) 147–150

Cervical spinal interbody fusion with Kiel bone

P. S. RAMANI, R. M. KALBAG AND R. P. SENGUPTA*

SUMMARY

Experience with the use of the Kiel bone graft in anterior cervical interbody fusion in cervical spondylosis is reported. The survey reviews the results of operations on 73 disc spaces in 65 consecutive patients, from 2 to 5 years after the operation. We have failed to confirm that any bony fusion in the true sense occurs with Kiel bone in anterior cervical interbody fusion. However, the aims of the operations are achieved, namely removal of the disc and osteophyte, fixation of the spine to prevent compression of the neural tissues, distraction of the adjacent vertebral bodies providing increased room in the intervertebral foramina and stability of the spine.

INTERBODY fusion of the cervical spine by an anterior approach using the Cloward technique (Cloward, 1958) is now one of the standard operations in surgery. In the early stages of our experience of the operation, in common with that of others using autografts from the iliac crest, there was a higher degree of morbidity from the donor site than anticipated. Discomfort in the area involved, often amounting to pain, was a consistent factor delaying discharge from hospital and prolonging convalescence. Change to an alternative source for the graft was prompted for a reason peculiar to the Regional Neurological Centre, Newcastle upon Tyne, where a prospective study of the relative merits of the various methods of management of cervical spondylotic myelopathy is in progress (Kalbag, 1972). Serial functional assessment of the patients was one of the basic features in the study, and it was considered that pain from the donor site would introduce a bias by reducing the timed performance figures for the Cloward group.

Commercially produced heterografts have been available for many years but are still viewed with reservation. It was, however, felt that as far as the treatment of degenerative disc disease was concerned, such grafts were worth consideration.

Kiel bone is a processed animal bone prepared from young calves. It was introduced in 1957 (Maatz and Bauermeister, 1957). It is partially deproteinized and according to the authors it is substituted by living bone faster and more completely than any other bone grafts.

Materials and methods

We have used Kiel bone since June 1968 in over 150 patients, but this survey reviews the results in only 65 consecutive cases from 2 to 5 years after the operation, thus giving a follow-up period of at least 2 years. Seventy-three disc spaces were dealt with in these 65 cases, 8 of which required fusion at two levels. There were 55 males and 10 females and 77 per cent of the cases were in the fifth or sixth decade. The operation was carried out using the standard Cloward technique (Cloward, 1958, 1962) with the patient in Halter traction. The drill hole straddling the disc was made with a 12·5-mm drill and the dowel inserted was 15·5 mm in diameter. A closed suction drain was left routinely in the prevertebral space for 24 hours. No collar was provided for postoperative immobilization of the neck. Apart from paraparetic patients who required intensive physiotherapy, patients were discharged home on the fifth day. Check X-rays of the cervical spine were taken the day after operation, at 6 weeks and then at 6-monthly intervals. We attempt to countersink the dowel slightly or make it flush with the bodies. In 9 patients, however, the first postoperative check X-rays showed the dowel to be slightly protruding forwards beyond the anterior surface of the vertebral bodies (*Fig.* 1*a*). Without immobilization in a collar, follow-up X-rays showed normal alignment and stability indistinguishable from that of a more satisfactorily placed dowel (*Fig.* 1*b*, *c*).

Results

Fifty-six (86 per cent) cases showed satisfactory alignment of the spine without abnormal mobility in flexion or extension at the time of final assessment. In 2 cases the dowel had to be removed because of infection, and the remaining 7 cases showed some complications as described below.

Partial absorption of the Kiel bone dowel was noted in 4 patients at 6 weeks' follow-up, but they had no symptoms. All the same, immobilization in a collar was carried out for 3 months.

Partial resorption of the vertebral bodies adjacent to the graft was seen in 3 patients at the end of 6 weeks, but with a collar alone stability and fixation were obtained.

Fracture of adjacent vertebral bodies was not a feature using autografts but occurred in 2 cases while a Kiel bone was being hammered in, when the anterior edge of one of the adjacent vertebrae was chipped off. This complication occurred in patients with some degree of osteoporosis and marked spondylotic changes. The contributory factor was probably the hard consistency of Kiel bone. Perhaps with the extension of the neck, as recommended by Cloward, this complication could have been avoided, but in our series, where a narrow spinal canal and myelopathy were frequent, extension of the neck under general anaesthesia was considered undesirable because of the obvious hazards of such a manœuvre.

---

* Regional Neurological Centre, Newcastle General Hospital, Newcastle upon Tyne.

graft, which with a diameter of 15·5 mm seems too large for easy introduction into a drill hole 12·5 mm in diameter, especially where the spine shows gross osteophyte formation. Taheri and Gueramy (1972) use a 14-mm dowel where only one space is operated upon and a 12-mm dowel if more than one space warrants attention. The former size would seem preferable to the one we have used.

In conclusion we have failed to confirm that any fusion in the true sense occurs with Kiel bone in cervical interbody fusion; nevertheless, we feel that except in fracture dislocation there is no practical disadvantage in its use and that the saving in operation time and morbidity more than counters any objections to its use in the particular context of cervical spondylotic disease.

Acknowledgement

We wish to acknowledge the help of the Department of Neuroradiology, Newcastle General Hospital, for providing the X-rays.

References

BURWELL R. G. (1969) The fate of bone grafts. In: APLEY A. G. (ed.) *Recent Advances in Orthopaedics.* Baltimore, Williams & Wilkins, pp. 115–208.

CLOWARD R. B. (1958) The anterior approach for removal of ruptured cervical discs. *J. Neurosurg.* **15**, 602–617.

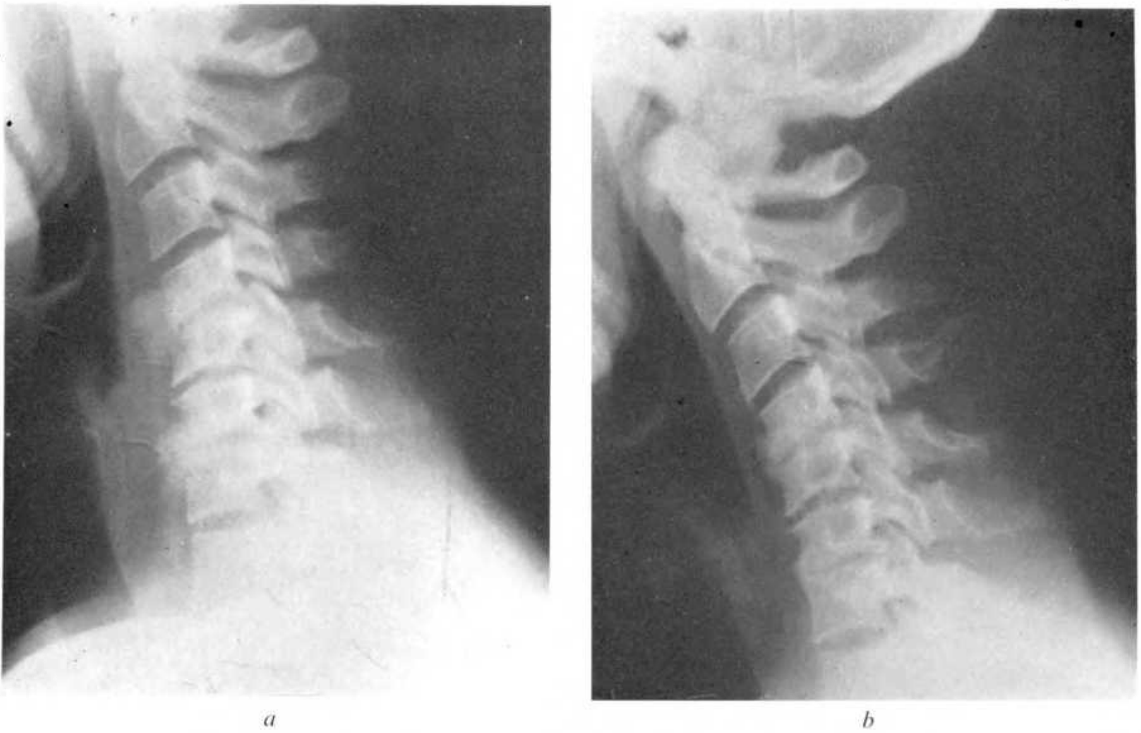
CLOWARD R. B. (1962) New method of diagnosis and treatment of cervical disc disease. *Clin. Neurosurg.* **8**, 93–132.

KALBAG R. M. (1972) Notes and comments on cervical spondylosis. *Br. Med. J.* **1**, 563.

MAATZ R. and BAUERMEISTER A. (1957) A method of bone maceration. Results in animal experiments. *J. Bone Joint Surg. (Am.)* **39**, 153–166.

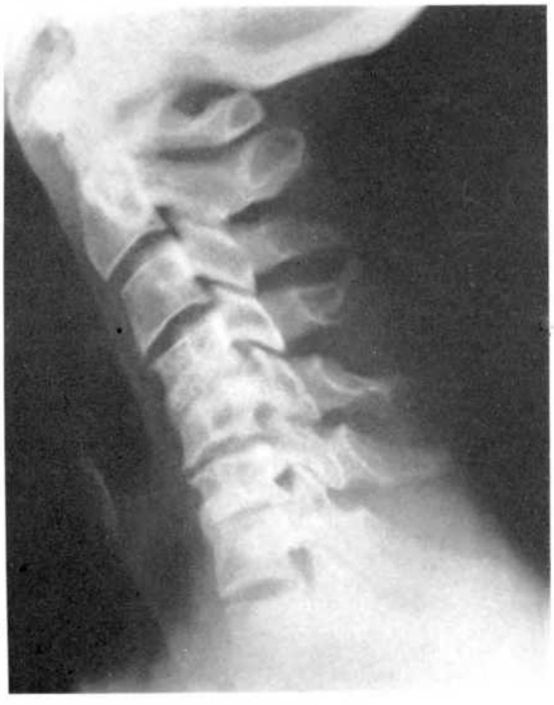
ROBINSON R. A., WALKER A. E., FERLIC D. C. and WIECKING D. K. (1962) The results of anterior interbody fusion of the cervical spine. *J. Bone Joint Surg. (Am.)* **44**, 1569–1587.

TAHERI Z. E. and GUERAMY M. (1972) Experience with calf bone in cervical interbody fusion. *J. Neurosurg.* **36**, 67–71.



a

b



c

Fig. 1. *a*, Lateral X-ray of the cervical spine taken immediately after operation shows anterior protrusion of the dowels which is more marked at the upper level (C4/5). However, follow-up X-rays taken (*b*) 8 months and (*c*) 17 months after the operation show alignment and stability indistinguishable from that of a more satisfactorily placed dowel.

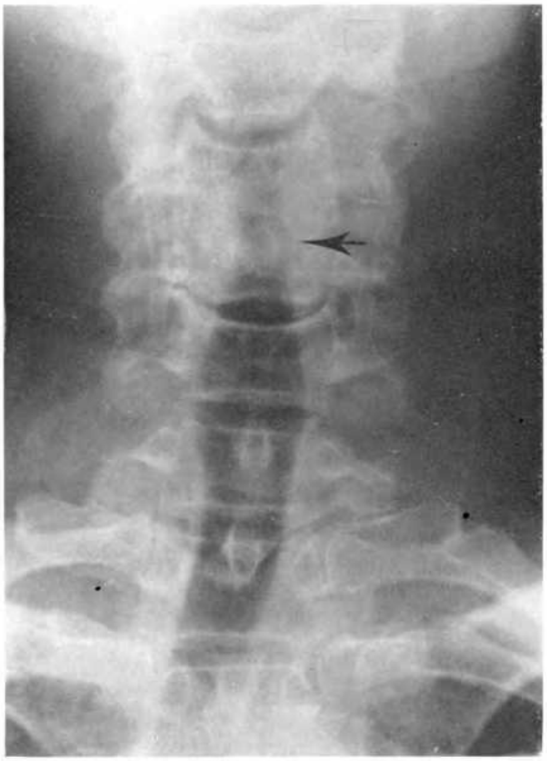
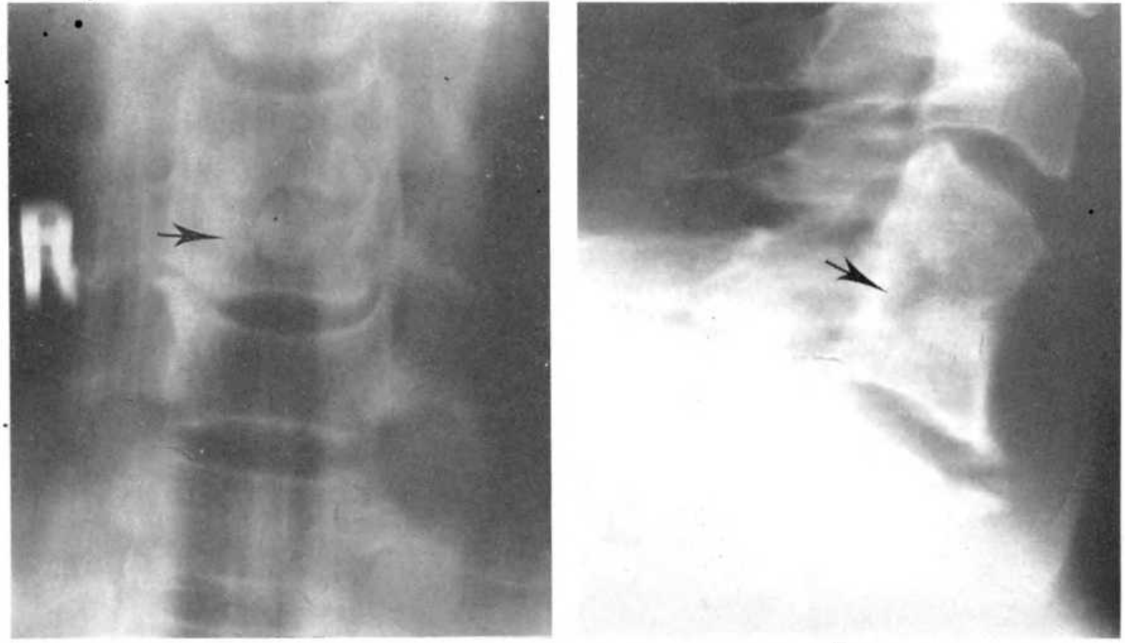


Fig. 2. Anteroposterior X-ray of the cervical spine taken 2 years after operation shows a halo around the dowel.



a *b*

Fig. 3. *a*. Anteroposterior tomogram of the cervical spine 2 years after the operation and (*b*) lateral tomogram of the cervical spine nearly 5 years after operation showing a halo around the dowel and indicating the absence of fusion.

All cases with partial absorption of the dowel as well as the adjacent vertebral bodies also showed some later anterior protrusion of the dowel.

In all these 7 cases immobilization in a collar was carried out. The end result was a stable spine although all of them showed some angulation of the spine.

A radiological study of our cases does not show a single case in which one could say with any confidence that bony fusion had occurred. Some patients showed a halo around the dowel (*Fig*. 2) even at the end of 5 years. Those who did not show the halo on plain X-rays were submitted to tomography in two planes and all of them showed a distinct halo surrounding the dowel (*Fig*. 3). We have interpreted this halo as a zone of fibrous tissue encaging the graft. We cannot therefore confirm that fusion occurs with the use of Kiel bone.

Discussion

Cloward (1962), reporting his experience with cadaver bone, thought that the common belief that autologous bone is superior to homologous bone was untenable. Burwell (1969), in a most comprehensive review of the fate of bone grafts, concluded that the best bank bone for clinical use seemed to be the freeze-dried homologous cancellous bone sterilized by irradiation. However, Taheri and Gueramy (1972), reporting on 200 cases with cervical disc disease who were operated on using the Cloward technique, stated that with heterogenous bone the results are good, the operation time is shortened and complications are diminished. They graded their patients radiologically into 'excellent', defined as good fusion and no angulation, while 'good' implied sound fusion but minimal angulation; 85·5 per cent were considered excellent and 11·5 per cent good, indicating that fusion or bony union had occurred in 97 per cent. This compares very favourably with the results quoted by Robinson et al. (1962). Admittedly, like the present series, this was a smaller series of 55 cases in which ileal autografts were used with an approximately 88 per cent fusion rate. A radiological study of our own cases does not show a single case in whom one could say with any confidence that bone fusion had occurred.

However, the absence of true fusion does not show any material disadvantages in the particular situation that we are considering, namely cervical disc disease, where spinal instability such as in fracture dislocation is rare. Our series shows 'satisfactory' results in 86 per cent in that alignment and stability have been achieved without convincing evidence of fusion. As designed for the spine, the Cloward operation using a dowel 3 mm larger than the drill hole provides firm splinting and with the resultant close approximation to a bed of vascular cancellous bone. Even with merely the splinting effect at the site of operation, the aims of the particular procedure are achieved, i.e. (1) removal of the disc and osteophyte, (2) fixation of the spine and (3) distraction of the adjacent vertebral bodies providing increased room in the intervertebral foramina. In this respect the results appear to be superior to those of autografts; Robinson et al. (1962) found abnormal mobility in flexion and extension in 9 out of the 56 patients reported.

Mechanical damage to the adjacent vertebral bodies could be related to the consistency and size of the

Br. J. Surg. Vol. 62 (1975) 151–164

Surgical Research Society

A meeting of the Surgical Research Society was held in King's College Hospital, London, on 3 and 4 January 1975 with Professor A. P. M. Forrest (President of the Surgical Research Society) in the chair. The following papers were presented:

1. An *in vivo* test of immune responsiveness in man

J. R. SALAMAN and D. MILLAR, *Institute of Renal Disease, Cardiff Royal Infirmary*

A test has been devised with the object of assaying immune responsiveness in normal and immunodepressed persons and is based on the graft-versus-host model of Ford et al. (1970) and employs rat antigens as the immunological stimuli. Peripheral blood lymphocytes were injected into the hind feet of young Wistar rats; 7 days later the popliteal lymph nodes were removed and weighed. It was found that the unwanted host-versus-graft activity could be suppressed in the rats by total body irradiation, 300 rad being the optimum dose. Inactivated lymphocytes were injected into the right hind foot as a control. Inactivation by irradiation (2400 R) was not completely successful and formolization was found to be a more satisfactory alternative.

In each test formolized and unformolized cells (in the same dose) were injected into the right and left hind feet respectively and the result expressed as a ratio—weight of left node : weight of right node. Lymphocytes from 45 healthy individuals were examined in this way. Experiments were performed in triplicate and the mean ratio plotted against the dose of cells injected. A close linear correlation was found ($r = 0{\cdot}86$) which could be expressed as:

$$\log \text{response} = 0{\cdot}234 + 0{\cdot}741 \log \text{dose} \pm 0{\cdot}538.$$

All normal individuals reacted similarly and a 'poor responder' group could not be identified. However, patients with immune depression could be shown to be statistically distinct.

FORD W. L., BURR W. and SIMONSEN M. (1970) A lymph node weight assay for the graft-versus-host activity of rat lymphoid cells. *Transplantation* 10, 258–266.

2. Effect of revisional surgery for vasomotor dumping on kinin release

A. CUSCHIERI, KAREN J. WORTHINGTON and BARBARA MASON, *Department of Surgery, University of Liverpool*

A controlled clinical trial of isoperistaltic versus antiperistaltic jejunal interposition for severe vasomotor dumping is in progress in Liverpool. To date 17 patients have been admitted to the trial. The effect of surgery on kinin release has been studied in patients who were rendered symptom-free by surgery (group A, $n = 11$) and others who were not improved (group B, $n = 6$). Kinin results are expressed in ng/ml as the mean ± standard error.

Each patient was given a hypertonic glucose meal (100 g) before the operation and in all 17 patients a dumping attack was diagnosed. Peripheral venous blood was taken before the attack and at the height of the vasomotor symptoms. The blood was extracted for estimation of the free bradykinin activity (Talamo et al., 1969), which was assayed on the isolated rat uterus. Haematocrit estimations were also performed. The hypertonic glucose test was repeated 3 months after surgery, except that in the patients who did not dump at this stage blood was taken before and 30 minutes after the glucose meal.

The resting preoperative venous kinin was $1{\cdot}89 \pm 0{\cdot}50$ ng/ml in group A patients and $1{\cdot}30 \pm 0{\cdot}35$ ng/ml in group B patients ($P > 0{\cdot}05$). However, this rose to $56{\cdot}15 \pm 11{\cdot}9$ ng/ml after glucose administration in group A cases compared with $3{\cdot}65 \pm 2{\cdot}33$ ng/ml in group B ($P < 0{\cdot}01$). At 3 months after operation the kinin level after a glucose meal was $4{\cdot}18 \pm 1{\cdot}20$ ng/ml in group A. This was significantly lower than the preoperative level in the same group during a dumping attack ($P < 0{\cdot}01$) and similar to the fasting level at 3 months after surgery.

These results indicate that patients labelled as vasomotor dumping syndrome do not form a homogeneous group. Moreover, a preoperative demonstration of kinin release during an attack provoked by hypertonic glucose is indicative of a successful outcome after revisional surgery for the dumping syndrome.

TALAMO R. C., HABER E. and AUSTEN K. F. (1969) A radioimmunoassay for bradykinin in plasma and synovial fluid. *J. Lab. Clin. Med.* 74, 816–827.

3. Measurement of Po_2 in normal and ischaemic human skin

V. A. SPENCE and W. F. WALKER, *Department of Surgery, Ninewells Hospital, Dundee*

Monitoring of tissue Po_2 may play an important role in estimating the degree of shock and response to therapy. In view of the shortcomings of existing electrodes we developed a micro-electrode suitable for measuring skin Po_2 in man with excellent reproducibility and stability.

The mean skin Po_2 in 15 controls using 71 electrodes was 34 ± 5 mm Hg. A rapid increase to about three times the control value followed oxygen administration, with an equally rapid decline when oxygen was stopped.

The relationship of Po_2 to skin blood flow was determined using ^{133}Xe.

Patients with peripheral vascular disease served as a stable model for shock. The skin Po_2 was measured in the limbs of 20 patients, each acting as his own control. In severe ischaemia the Po_2 was 20 mm Hg or less and the response to oxygen was nil. The response varied with the degree of ischaemia. In the reversible situation Po_2 and skin blood flow improved following operation.

It is concluded that the micro-electrode designed is stable and gives reproducible results; the control Po_2 is a good guide to tissue blood flow; the Po_2 gradients provide valuable information on changes in blood flow and oxygen metabolism; and, finally, the electrode is suitable for studies in shock now in progress.

4. Pregnenolone metabolism as a prognostic guide in human mammary carcinoma

N. J. O'HIGGINS, N. DESHPANDE and PAMELA CARSON (J. L. BOAK), *Department of Surgery, Royal Postgraduate Medical School, and Imperial Cancer Research Fund*

Low plasma concentrations and urinary excretion of androgens may be associated with poor response to endocrine treatment in patients with advanced breast cancer (Brownsey et al., 1972) cortisol levels may also be raised in advanced disease (Jensen et al., 1968).

Pregnenolone is converted to androgen and cortisol. It was considered that the conversion rate of pregnenolone to androgen might be reduced and the conversion rate to cortisol increased in unresponsive patients with advanced mammary cancer.

After a bolus injection of 10 μCi, 40 μCi of tritium-labelled (^{3}H) pregnenolone in saline were infused intravenously for 4 hours through an electrically driven pump. Hourly plasma samples were analysed by paper chromatography for concentrations of radioactive pregnenolone, cortisol and the androgen dehydroepiandrosterone (DHA).

In 45 patients the ratio of DHA to cortisol was similar in those with early and advanced disease. Of 26 patients with advanced disease, the DHA : cortisol ratio was significantly ($P<0{\cdot}01$) lower in the 19 patients who failed to respond to endocrine treatment (mean ratio 0·548) when compared with the 7 who responded favourably (mean ratio 1·1).

ACTH increased the concentration of cortisol and DHA, but did not alter the DHA : cortisol ratio significantly.

Reduced conversion of pregnenolone to DHA probably explains the low androgen levels observed in unresponsive mammary cancer.

BROWNSEY B., CAMERON E. H. D., GRIFFITHS K., GLEAVE E. N., FORREST A. P. M. and CAMPBELL H. (1972) Plasma dehydroepiandrosterone sulphate levels in patients with benign and malignant breast disease. *Eur. J. Cancer* **8**, 131–137.

JENSEN V., DESHPANDE N., BULBROOK R. D. and DOOUSS T. W. (1968) Adrenal function in breast cancer: production and metabolic clearance rate of cortisol in patients with early or advanced breast cancer and in normal women. *J. Endocrinol.* **42**, 425–432.

5. The relationship between alcohol and head injury and its effect on the conscious level

S. GALBRAITH, W. R. MURRAY, A. R. PATEL and R. KNILL-JONES (W. B. JENNETT), *The University Departments of Surgery, Medicine and Neurosurgery, The Institute of Neurological Sciences, Glasgow, and The Western Infirmary, Glasgow*

Recent intake of alcohol may complicate assessment of the conscious level after head injury and may make it difficult to recognize the development of complications such as intracranial haematoma. Of 200 consecutive traumatic intracranial haematomas, 72 (36 per cent) had been deteriorating for more than 12 hours before being referred to the Department of Neurosurgery; in half of these alcohol was a confusing factor. The extent to which alcohol contributes to the problem of head injuries and their assessment was explored by measuring alcohol levels in 400 consecutive head injuries admitted to general surgery wards. The relationship between the blood alcohol and conscious state was assessed using the Glasgow coma scale (Teasdale and Jennett, 1974).

Recent alcohol consumption was suspected clinically in 224 (56 per cent) of head injuries and in 75 per cent of males over the age of 18 years. In these the mean blood alcohol level was 193 mg per cent (maximum 375 mg per cent). As a cause of injury, road accidents were only marginally more common (108, 27 per cent) than assaults (98, 24·5 per cent) and 'falls under the influence' (92, 23 per cent). Mean alcohol levels were higher for 'falls under the influence' (189 mg per cent) than assaults (121 mg per cent) and road traffic accidents (58 mg per cent). These differences are significant.

Of the patients with recent alcohol intake, 328 (82 per cent) were fully conscious on the coma scale, the mean blood alcohol level being 134 mg per cent. Disorientation was observed in 68 (17 per cent) in whom the mean blood alcohol was 203 mg per cent. These differences are significant. Only 4 could be described as 'in coma', the mean blood alcohol being 326 mg per cent.

These results indicate that many patients with head injury in Glasgow have recently taken considerable quantities of alcohol. The level is related to the way in which the injury occurred, and alcohol is probably an important causative factor. High levels are necessary before the conscious level is affected and coma results only at levels greater than 300 mg per cent.

TEASDALE G. and JENNETT W. B. (1974) Assessment of coma and impaired consciousness. *Lancet* **2**, 81–84.

6. Haemostasis and healing following median sternotomy

T. G. J. BRIGHTMORE (C. WASTELL), *Thoracic Surgical Unit, Westminster Hospital, London*

Following median sternotomy the standard method for securing haemostasis is bone wax. Examination of sterna from 6 patients who died up to 5 years after sternotomy has demonstrated an obstructive effect of the wax on healing.

To find a haemostatic without this adverse effect, median sternotomy was performed on 83 goats. The animals were divided into six groups and sternal blood loss was measured over two 15-minute periods. In each group the haemorrhage was unchecked in the first period. In the second it continued unchecked in the control group (22), but in the other groups haemostasis was attempted with wax (12), collagen (11), isobutyl-cyanoacrylate (15), collagen and isobutyl-cyanoacrylate (12) and an autologous red cell compound devised for this study (11). Sixty-two animals survived. The animals were sacrificed at intervals from 1 day to 6 months. Sternal transverse sections were photographed, X-rayed and examined microscopically. A scoring system based on the microscopy was used to measure sternal healing.

Differences in blood loss per unit sternal area in the first period between groups could not be shown to be significant. In the second period analysis of variance shows that the blood loss per unit area in the control group was significantly higher than in the treated groups (for $F(7;\ 70)$, $P<0{\cdot}001$), but a significant difference between treated groups could not be shown. However, wax and the red cell compound were superior, taking into account ease of application. The obstructive defect in healing with wax was not seen with the autologous red cell compound. The latter is proposed as a sternal haemostatic and its effect on human sterna has been tested in 6 patients with favourable results.

7. Gastro-intestinal hormonal responses following massive small bowel resection

A. A. B. BARROS D'SA, T. L. KENNEDY, K. D. BUCHANAN and T. G. PARKS, *Departments of Surgery and Medicine, The Queen's University and Royal Victoria Hospital, Belfast*

Are humoral mechanisms responsible for hypermotility and gastric hypersecretion which are recognized sequelae of massive small bowel resection?

The effect of a fat meal on circulating gastro-intestinal hormones was assessed in dogs before and after 75 per cent small bowel resection. The following hormones were measured by radio-immunoassay: insulin, gastrin, secretin, total glucagon-like immunoreactivity (GLI) and pancreatic glucagon.

In 9 conscious dogs resection produced significant falls in basal and stimulated levels of total GLI in peripheral venous blood ($P<0{\cdot}05$) and insignificant rises in basal and stimulated gastrin values. Secretin levels fell minimally.

To clarify the source of the GLI further, acute experiments were undertaken with 5 anaesthetized dogs in each of the following groups: (*a*) laparotomy; (*b*) resection; (*c*) resection and total pancreatectomy; (*d*) pancreatectomy.

Following resection alone stimulated gastrin levels rose ($P<0{\cdot}05$), but when resection was combined with pancreatectomy the rise was more sustained ($P<0{\cdot}05$). Pancreatectomy alone was without effect on gastrin secretion.

Resection in anaesthetized dogs confirmed a reduction of total GLI, especially when pancreatectomy was added ($P<0{\cdot}05$). Pancreatectomy alone depleted total GLI by 83·5 per cent ($P<0{\cdot}001$) and pancreatic glucagon by 91 per cent ($P<0{\cdot}001$).

These hormonal abnormalities may be relevant to the pathophysiology of massive small bowel resection and support the concept that an enteric islet cell axis for fats may exist.

8. Highly selective vagotomy for duodenal ulcer: is antrectomy needed for the hypersecretors?

I. R. PICKFORD, D. JOHNSTON, B. E. WALKER and J. C. GOLIGHER, *University Department of Surgery, The General Infirmary, Leeds*

Kronborg (1972) has suggested that duodenal ulcer patients with a maximum acid output (MAO) greater than 46 mEq/hr (M), or 42 mEq/hr (F) should have antrectomy added to vagotomy, because after vagotomy and drainage recurrent ulceration was found in 14 per cent of hypersecretors, but in only 2 per cent of normal secretors. For similar reasons, Robbs et al. (1973) recommended vagotomy and antrectomy for duodenal ulcer patients with MAO > 25 mEq/hr.

Since highly selective vagotomy (HSV) is even more conservative than vagotomy and drainage we were interested to find out whether 'hypersecretors' (peak acid output > 50 (M) and > 40 (F) mEq/hr) had worse clinical results after HSV than 'normal secretors'. Results in 40 hypersecretors were compared with those of 60 normal secretors 2–6 years after HSV. Mean ages (42 years), and the incidence of incomplete vagotomy (6 per cent) were equal in the two groups.

Results for hypersecretors compared with normal secretors were: Visick grades 1+2, 85 per cent versus 88 per cent; proved recurrent ulcer, both 0 per cent; ulcer-type pain (often transient), both 7 per cent; diarrhoea, both 4 per cent; early dumping, 1 per cent versus 7 per cent ($P = 0{\cdot}054$); other symptoms, no significant difference.

These results suggest that HSV is adequate surgical treatment for patients who have duodenal ulcer and very high acid output. Antrectomy does not seem to be necessary, provided that the incidence of incomplete vagotomy can be kept low.

KRONBORG O. (1972) Influence of the number of parietal cells on risk of recurrence after truncal vagotomy and drainage for duodenal ulcer. *Scand. J. Gastroenterol.* **7**, 423–431.

ROBBS J. V., BANK S., MARKS I. N. and LOUW J. H. (1973) Selection of operation for duodenal ulcer based on acid secretory studies: a reappraisal. *Br. J. Surg.* **60**, 601–605.

9. Glucose tolerance and insulin secretion after selective gastric vagotomy and pyloroplasty

R. BITTNER, H. G. BEGER, E. KRAAS and R. ROSCHER, *Department of Surgery, Klinikum Charlottenburg, Free University, Berlin*

Hyperglycaemia following oral glucose load in patients after truncal vagotomy and pyloroplasty is well documented (Thomford et al., 1974). The influence of selective gastric vagotomy and pyloroplasty (SGV+P) on glucose tolerance and insulin secretion remains unclear.

In the early postoperative period (days 6–10) 19 glucose infusion tests (GIT) and 16 oral glucose tests (OGT) were performed in 10 patients after SGV+P and in 12 control patients after abdominal surgery. To obtain more precise information blood samples were taken simultaneously from the portal vein and one cubital vein (Bittner et al., 1973).

The mean disappearance rate of glucose (k value) as well as the pattern and area below the insulin concentration curve (ΔIRI) are nearly identical in both test groups (SGV+P: $k = 0{\cdot}94$, ΔIRI (portal vein) = 18 702·5; control: $k = 1{\cdot}02$, ΔIRI (portal vein) = 18 401).

Glucose (mg/100 ml)

	Fasting	60 min	120 min	180 min
SGV+P*	74 ± 9	130 ± 31	107 ± 19	92 ± 12
Control*	86 ± 13	171 ± 43	162 ± 50	132 ± 42
	$P < 0{\cdot}05$	$P < 0{\cdot}025$	$P < 0{\cdot}01$	$P < 0{\cdot}025$

Insulin (μu./ml portal vein)

	Fasting	30 min	60 min	90 min	150 min
SGV+P*	37 ± 36	113 ± 63	79 ± 52	53 ± 26	36 ± 16
Control*	27 ± 15	49 ± 22	82 ± 46	103 ± 46	86 ± 56
	NS	$P < 0{\cdot}01$	NS	$P < 0{\cdot}01$	$P < 0{\cdot}025$

* $n = 8$. NS, No significance.
Insulin levels in the cubital vein showed no significant differences.

In patients with SGV+P the responsiveness of the β-cells to glucose stimulation is not altered. In addition, the oral glucose tolerance is more nearly normal compared with the control patients. The peak concentration of insulin is reached more rapidly. These results lead to the conclusion that in man after an oral glucose load SGV+P intensely provokes the release of an intestinal factor which is a potent stimulator of insulin secretion.

BITTNER R., BEGER H. G., KRAAS E. and GERHARDS E. (1973) Untersuchung des Glucosestosswechsels nach selektiver Vagotomie und Pyloroplastik. *Langenbecks Arch. Chir.* Suppl. Chirurgisches Forum für experimentelle und klinische Forschung, pp. 259–262.

THOMFORD N. R., SIRINEK K. R., CROCKETT S. E., MAZZAFERRI E. L. and CATALAND S. (1974) Gastric inhibitory polypeptide. *Arch. Surg.* **109**, 177–182.

10. Effect of proximal gastric vagotomy and total vagotomy on the co-ordination of electrical activity of the stomach and duodenum

P. AEBERHARD and B. S. BEDI, *Department of Surgery, Western Infirmary, Glasgow*

Gastric retention occurs following total vagotomy alone. One of the reasons for this retention may be the lack of co-ordination of the motor activity between the stomach and duodenum. As electrical activity can be used to monitor the motor activity of the gastro-intestinal tract, experiments were designed to study the effect of proximal gastric vagotomy (PGV) and total vagotomy (TV) on the co-ordination of the electrical activity across the gastroduodenal area.

The electrical activities from the antrum and duodenum were recorded using monopolar silver–silver chloride electrodes in 4 fully conscious mongrel dogs. The recordings were made after ingestion of a meat meal. After a control study PGV was performed and the recordings repeated. Approximately 8 weeks later, total vagotomy was carried out and the records made. A method of cross-correlation was applied to the electrical recordings obtained before and after the vagotomy.

The relationship between the antral pacesetter potential and the occurrence of duodenal action potentials was observed in the control studies and this co-ordination persisted following PGV and TV.

The results of this study suggest that PGV and TV have no effect on the co-ordination of the motor activity of the stomach and duodenum.

11. A dumping provocation test

C. LAWSON-SMITH and J. P. S. THOMSON (M. HOBSLEY), *Department of Surgical Studies, The Middlesex Hospital, London*

The dumping syndrome is a common sequela to gastric surgery. In most patients it is readily diagnosed, but there are exceptions. Our findings with a test designed to provide an objective diagnosis of dumping are reported.

The fasting patient, lying semi-recumbent, drank 200 ml 50 per cent glucose. Symptoms were noted and the plasma volume fall estimated from serial haematocrit measurements (Le Quesne et al., 1960).

One hundred and twenty-five patients were studied after operations for peptic ulceration (partial gastrectomy 33, truncal vagotomy 43, selective vagotomy 31, proximal gastric vagotomy 18).

The patients fell into three *clinical* groups:

1. Asymptomatic (54). Of these, 40 experienced no symptoms during the test.
2. 'Dumpers' (63). All had dumping symptoms during the test.
3. Those with abdominal pain suggestive of recurrent ulceration (8). Six experienced their pain during the test and had a large plasma volume fall (15·5 ± 1·4 (s.e.m.) per cent), thereby establishing a diagnosis of dumping. The other 2 were asymptomatic during the test and a recurrent ulcer was later confirmed in both.

Thirty-four of the 42 patients who were asymptomatic during the test had a plasma volume fall of less than 9 per cent, whilst 79 of the 83 patients with dumping symptoms during the test had a fall of 9 per cent or more.

This test provided objective evidence of dumping, and it is of value in assessing patients with symptoms after gastric surgery.

LE QUESNE L. P., HOBSLEY M. and HAND B. H. (1960) The dumping syndrome—1. Factors responsible for the symptoms. *Br. Med. J.* **1**, 141–147.

12. The coexistence of dumping and duodenogastric reflux

I. A. DONOVAN, M. R. B. KEIGHLEY, D. W. GRIFFIN, L. K. HARDING and J. ALEXANDER-WILLIAMS, *The General Hospital and Dudley Road Hospital, Birmingham*

The symptomatic sequelae induced by gastric operations are notoriously complex. They are usually associated with gastric retention, early rapid passive gastric emptying (cascading or gastric incontinence) or duodenogastric reflux. First impressions would suggest that cascading and reflux would not occur together; however, clinical experience suggests that they may.

In a prospective randomized trial 20 patients with duodenal ulceration were studied before operation and 9 after proximal gastric vagotomy (PGV) and 11 after truncal vagotomy and antrectomy (TV+A). Emptying of solid and liquid meals was measured by γ scintiscanning (^{113}In). Reflux was studied radiologically (Capper et al., 1966) and by measuring bile pigment concentrations in residual and basal gastric aspirate.

After PGV 3 patients cascaded liquids and 1 had reflux. None had both abnormalities. After TV+A, 9 patients cascaded liquids and 6 had reflux. Five both cascaded and refluxed. Furthermore, in 3 of these 5 patients delayed active emptying was also present ($T_{\frac{1}{2}}>80$ minutes).

Therefore, bile reflux does occur in patients who cascade, and the refluxed bile may remain in contact with the gastric mucosa for a long time. These findings emphasize the importance of the antropyloric mechanism as a two-way sphincter.

CAPPER W. M., AIRTH G. R. and KILBY J. O. (1966) A test for pyloric regurgitation. *Lancet* 2, 621–623.

13. Duodenal ulceration, gastric emptying, enteroglucagon release and abnormal oral glucose tolerance

C. LAWSON-SMITH, D. N. L. RALPHS, S. BLOOM and M. HOBSLEY, *Department of Surgical Studies, The Middlesex Hospital, London*

The greater rise in blood glucose produced by oral glucose in duodenal ulcer patients compared with controls (Humphrey et al., 1972) has been variously attributed to differences in rates of gastric emptying or enteroglucagon release. These possibilities have been investigated in 10 controls and 17 duodenal ulcer patients by measuring the half-life ($T_{\frac{1}{2}}$) of emptying of 200 ml 50 per cent glucose labelled with ^{113}In and estimating plasma enteroglucagon and blood glucose at intervals for 2 hours.

The rise in blood glucose concentration (106·8±6·6 (s.e.m.) mg/100 ml) in duodenal ulcer patients was greater ($t=3{\cdot}942$, $P<0{\cdot}001$) than in the controls (64·6±8·3 mg/100 ml). There were significant correlations between log $T_{\frac{1}{2}}$ and (*a*) the rise in blood glucose concentration ($r=0{\cdot}491$, $P<0{\cdot}05$) and (*b*) enteroglucagon release (Spearman's rho, $r_S=0{\cdot}4429$, $P<0{\cdot}05$). However, enteroglucagon release *did not* correlate with blood glucose. After the blood glucose increases were standardized for different rates of gastric emptying, the rise in blood sugar in the DU group (99·4±8·6 mg/100 ml) remained significantly greater ($t=3{\cdot}358$, $P<0{\cdot}005$) than in the controls (65·9±5·1 mg/100 ml).

It is concluded that the shape of the glucose tolerance curve in duodenal ulcer patients compared with controls is not related to enteroglucagon release and only partly to stomach emptying. The cause of the greater rise in blood glucose in duodenal ulcer patients has yet to be elucidated.

HUMPHREY C. S., DYKES J. R. W. and JOHNSTON D. (1972) Glucose tolerance and insulin secretion in patients with chronic duodenal ulcer. *Br. Med. J.* 4, 393–396.

14. The slowing of gastric emptying by intestinal hormones

M. MEVES, H. G. BEGER, U. HAUBOLD and B. HÜTHWOHL, *Departments of Radiology and Surgery, Klinikum Charlottenburg, Free University, Berlin*

The influence of gastro-intestinal hormones on motor function of the stomach in man has been clearly established. This investigation has been performed in 33 healthy volunteers to determine the alteration of the gastric emptying process by a 20-minute infusion of natural hog gastrin I (2 μg/kg body weight) or pentagastrin (6 μg/kg body weight) or GIH-secretin (75 u.) or glucagon (Lilly, 1 mg).

Gastric emptying was measured by a modification of the scintiscan technique (Griffith et al., 1966), using a ^{51}Cr-labelled semi-solid test meal. The hormones were infused intravenously with a constant speed during a 20-minute period (period II). The alteration of the emptying process compared with the emptying before (period I) and after (period III) the drug infusion represents the effect of the infused drug on gastric emptying. Therefore the patients served as their own controls.

	Percentage of emptying of test meal during period			
	I	II	III	Student's *t*-test (periods I and II)
Gastrin I	20·1	2·8	10·7	$P<0{\cdot}0025$
	±9·5	±2·1	±6·6	
Pentagastrin	20·5	2·2	9·9	$P<0{\cdot}0025$
	±10·5	±2·6	±7·5	
GIH-secretin	25·2	3·4	18·0	$P<0{\cdot}0001$
	±6·6	±3·2	±2·5	
Glucagon	19·8	0·7	11·7	$P<0{\cdot}0001$
	±9·2	±0·5	±7·5	

Although gastrin and pentagastrin stimulate antral motor activity, both slow the gastric emptying of ordinary food to a significant degree ($P<0{\cdot}0025$), probably by increasing the intraduodenal pressure. Secretin and glucagon were found to slow gastric emptying significantly ($P<0{\cdot}0001$), probably by inhibiting antral motor activity.

GRIFFITH G. H., OWEN G. M., KIRKMAN S. and SHIELDS R. (1966) Measurement of rate of gastric emptying using chromium-51. *Lancet* 1, 1244–1245.

15. Immunological status of rats with passively enhanced renal allografts

P. J. MORRIS (H. A. F. DUDLEY), *Nuffield Department of Surgery, University of Oxford, Radcliffe Infirmary*

The administration of DA anti-Lewis serum to DA rats at the time of transplantation of (DA×Lewis)F_1 renal allografts prevents rejection and results in indefinite survival of all animals (Fabre and Morris, 1972, 1973). The following experiments were designed to elucidate the mechanism of immunosuppression in these animals with long surviving grafts.

1. In DA recipients intravenous injection of 3×10^8 lymph node and spleen lymphocytes 32 weeks after transplantation did not result in rejection of the renal allograft.

2. DA serum from long surviving animals did not block the response of normal DA lymphocytes to (DA×L)F_1 lymphocytes in mixed lymphocyte culture (MLC), although known enhancing sera did.

3. DA lymphocytes from long surviving animals showed some diminution in response to (DA×L)F_1 lymphocytes in MLC.

4. Eight weeks after transplantation of (DA×L)F_1 kidney into 6 enhanced DA recipients with one of its own kidneys remaining, the (DA×L)F_1 kidney was removed. The animal's remaining kidney was removed 2, 4 or 8 weeks later and replaced with a new (DA×L)F_1 kidney (2 animals in each group). The new kidney was not rejected, all the animals surviving indefinitely.

These findings indicate that the continuing survival of passively enhanced renal allografts in this model is not due to blocking factors, and is better explained on the basis of specific clonal deletion or inactivation.

FABRE J. W. and MORRIS P. J. (1972) Experience with passive enhancement of renal allografts in a (DA×Lewis)F_1 to Lewis strain combination. *Transplantation* 13, 604–609.

FABRE J. W. and MORRIS P. J. (1973) Dose response studies in passive enhancement on rat renal allografts. *Transplantation* 15, 397–403.

16. Nature of cells removed from rejecting rat cardiac allografts

S. G. MACPHERSON, N. L. TILNEY, T. B. STROM and C. B. CARPENTER (D. N. H. HAMILTON), *Department of Surgery, Western Infirmary, Glasgow, and Departments of Medicine and Surgery, Harvard Medical School, Boston, Massachusetts, USA*

Cells infiltrating rat cardiac allografts have been studied *in vitro* with respect to their morphology and surface properties.

One hundred and six heterotopic heart transplants (Ono and Lindsey, 1969) were performed using BN or LBNF$_1$ rats as donors to Lewis recipients. Rejection, as measured by cessation of palpable beat, occurred at 7–9 days. The allografts were removed 3–8 days following transplantation and were diced, passed through a mesh, incubated with DNAase and the cells separated with Ficoll-Hypaque.

B cells with surface immunoglobulin were identified by fluorescein-labelled rabbit anti-rat IgG and comprised 47 per cent of the yield at days 3–4 and 35 per cent at days 5–6. At 3–4 days 43 per cent of cells had a surface receptor for the Fc fragment of immunoglobulin; 0·3 per cent of the harvested cells bound the C$_3$ component of complement and formed EAC rosettes.

Macrophages were identified using acridine orange stain and formed 14–24 per cent of the cell population.

T lymphocyte function was demonstrated in a lymphocyte-mediated cytotoxicity test using ^{51}Cr-labelled donor cells as targets. Lysis peaked at 33 per cent at day 4–5. It is presumed that the T cells constitute the 29–48 per cent of the population not previously identified.

T lymphocytes and macrophages therefore invade the rat cardiac allograft during rejection, but there is also a population of B lymphocytes, unusual in that they lack C$_3$ surface receptors.

ONO K. and LINDSEY E. S. (1969) Improved technique of heart transplantation in rats. *J. Thorac. Cardiovasc. Surg.* 57, 225–229.

17. Should preserved organs be continuously perfused?

L. S. AGRAWAL, I. L. ROSENBERG and G. R. GILES, *University Department of Surgery, St James's Hospital, Leeds*

The optimal conditions for organ perfusion are still uncertain, particularly in respect to perfusate constituents and perfusion dynamics. We have used the rat heart preservation model described by Calman and Bell (1972) to investigate and compare four perfusates in an attempt to preserve the hearts for 24 hours. The four solutions used were: K solution with Dextran (Calman and Bell, 1972), K solution with PPF, K solution with 4 per cent Ficoll and Tyrode's solution with 4 per cent Ficoll.

It did not prove possible to preserve hearts for 24 hours using a simple flush and storage at 4 °C with K solution containing either Dextran or PPF. However, 50 per cent of the hearts were preserved in this manner by K solution or Tyrode's solution with Ficoll. Each solution was then tested in four programmes of perfusion with groups of 10 hearts. Continuous perfusion for 24 hours did not preserve any of the 40 hearts tested and all hearts were grossly oedematous.

Intermittent perfusion was tested by: (*a*) perfusion of each heart for 2 minutes every hour (8 of 40 hearts preserved); (*b*) perfusion for 2 minutes every 2 hours (17 hearts preserved); (*c*) perfusion for 2 minutes every 6 hours (23 hearts preserved). In the last group 80 per cent of hearts preserved in Tyrode's solution with Ficoll and all 10 hearts preserved in K solution with Ficoll were successfully resuscitated.

The results suggest, for this animal model at least, that there does not seem to be any advantage in continuous perfusion and that intermittent flushing of the organ at infrequent intervals gives better results.

CALMAN K. C. and BELL P. R. F. (1972) Experimental organ preservation. *Br. J. Surg.* 59, 758–764.

18. Preservation of isolated pancreatic islets

J. FERGUSON, R. H. ALLSOPP, R. M. R. TAYLOR, I. D. A. JOHNSTON and F. LATIMER, *Department of Surgery, University of Newcastle upon Tyne*

Isolated pancreatic islets have been successfully transplanted to the testis and omentum in guinea-pigs (Ferguson and Scothorne, 1972). If islet cell transplantation has any part to play in the surgical management of diabetes mellitus, methods of harvesting and preservation need further study.

This report describes the histological changes associated with three methods of preservation: (*a*) simple cold storage in Hanks balanced salt solution at 4 °C; (*b*) organ culture of microdissected islets; (*c*) storage of islets in liquid nitrogen at −187 °C.

Isolated islets were obtained using a free-hand microdissection procedure. The islets were studied by light microscopy after staining with Gomoris's aldehyde fuchsin stain.

Forty per cent of islets stored at 4 °C for 24 hours showed histologically viable alpha and beta cells. At 48 hours approximately 10 per cent showed viable cells. At 72 hours all islets were necrotic.

Microdissected islets from mouse, rat and guinea-pig were successfully cultured for up to 28 days.

Histologically recognizable alpha and beta cells have been observed following 24 hours' storage at −187 °C.

Organ culture is a satisfactory method for the long term preservation of isolated pancreatic islets. In a few cases histological evidence of survival has been correlated with functional studies.

FERGUSON J. and SCOTHORNE R. J. (1972) Transplantation of the endocrine pancreas in guinea pigs. *Br. J. Surg.* 59, 316.

19. Perfusate lactic acidosis in the assessment of human cadaver kidneys

R. W. G. JOHNSON, R. M. R. TAYLOR, J. SWINNEY and F. O. BELZER, *Departments of Surgery, University of Newcastle upon Tyne, and University of California, USA*

Perfusion characteristics alone do not adequately measure pre-existing damage in human cadaver kidneys, especially those that have been stored on ice before perfusion.

In this study 112 human cadaver kidneys arriving at two transplant centres were assessed by measuring the accumulation of lactic acid in the perfusate during the first hour of continuous perfusion. Lactate was measured on a Boehringer ultraviolet test kit and expressed in mg/100 ml corrected to a perfusate volume of 400 ml.

Storage method	IF	MLC	DF	MLC	NF
Perfusion*	55	29·6±5	13	60·2±6	0
+ ice, perfusion†	11		30		3
Total	66		43		3

IF, immediate function; MLC, mean lactate concentration (mg %); DF, delayed function; NF, non-function.
* $n = 58$. † $n = 44$.
Range of lactate concentration (mg %):
Perfusion alone: nil.
Perfusion+ice perfusion: 70>100.

Sixty-eight kidneys were stored on perfusion alone. The mean duration of storage was 28±6 hours. Immediate function rate was 80 per cent.

Forty-four kidneys were stored initially in ice for up to 12 hours and then perfused. The mean total storage time in this group was 25±9 hours. Immediate function rate was 25 per cent and there was a 6 per cent primary non-function rate.

There was a highly significant difference in perfusate lactic acidosis between the kidneys which functioned immediately and those in which onset of function was delayed; the mean difference was 30·6 mg per cent ($t = 12\cdot9$, $P < 0\cdot001$). The lactate concentrations for the 3 non-functioning kidneys ranged from 70 to >100 mg per cent.

Measurement of perfusate lactic acidosis when taken in conjunction with perfusion characteristics will accurately predict pre-existing injury in human cadaver kidneys.

20. Evidence of gentamicin nephrotoxicity in patients with renal allografts

J. M. WELLWOOD, A. E. THOMPSON and J. R. TIGHE, *St Thomas's Hospital, London*

Using the sensitive fluorimetric technique for assay of urinary N-acetyl glucosaminidase (NAG) and beta-galactosidase (GAL), elevated enzyme levels have been demonstrated in patients with renal disease (Dance et al., 1970) and during the rejection of renal allografts (Wellwood et al., 1973). We observed striking elevations in urinary enzymes when patients with renal grafts were treated with gentamicin.

Male Wistar rats were kept in metabolic cages. Clean 24-hour urine specimens were collected daily. Differing doses of gentamicin were administered daily for differing periods of time. Elevations in urinary NAG and GAL and histological and ultrastructural changes in rat kidneys were caused when gentamicin was administered in human therapeutic doses.

Urinary enzymes became elevated between 1 and 3 days after the onset of 20 courses of gentamicin in 18 patients with renal allografts. Levels fell between 2 and 5 days after cessation of gentamicin.

The serum creatinine rose during 75 per cent of the courses and urinary protein increased during 65 per cent of the courses. The renal histological and ultrastructural changes induced by gentamicin in rats were found in human renal tissue.

The administration of gentamicin may cause a reduction in function of renal allografts.

DANCE N., PRICE R. G., CATTELL W. R., LANSDELL J. and RICHARDS B. (1970) The excretion of N-acetyl-beta-glucosaminidase and beta-galactosidase by patients with renal disease. *Clin. Chim. Acta* **27**, 87–92.

WELLWOOD J. M., ELLIS B. G., HALL J. M., ROBINSON D. and THOMPSON A. E. (1973) Early warning of rejection? *Br. Med. J.* **2**, 261–265.

21. The action of subcutaneous and intravenous *Corynebacterium parvum* on the 'lymphocyte trap'

D. N. H. HAMILTON and ELISABETH BRADY, *Department of Surgery, Western Infirmary, Glasgow*

Corynebacterium parvum, a potent anti-tumour agent, powerfully attracts lymphocytes to the lymph nodes draining its site of subcutaneous injection. This activation of the 'lymphocyte trap' has been suggested to be the mechanism by which *C. parvum* acts against experimental tumours (Frost and Lance, 1973).

To test this hypothesis *C. parvum* was injected intravenously or subcutaneously into the foreleg of CBA mice, and tumours were then induced in the muscle of the same foreleg with Moloney sarcoma virus (MSV). Syngeneic lymphocytes labelled with ^{51}Cr were then injected intravenously at regular intervals after tumour induction, and as expected subcutaneous *C. parvum* produced a fourfold increase in the lymphocytes migrating to the draining lymph node. Subcutaneous *C. parvum*, however, produced only a 26 per cent reduction in the incidence of the MSV tumours. Intravenous *C. parvum* produced no change in the migration of lymphocytes to the node draining the tumour, but completely prevented the appearance of tumours.

By studying these two routes of administration, the anti-tumour activity of *C. parvum* is only seen with the intravenous route and its stimulation of the trap only with the subcutaneous route. Thus, *C. parvum* does not act on tumours via the 'lymphocyte trap'.

FROST P. and LANCE E. M. (1973) In: KNIGHT JULIE and WOLSTENHOLME S. E. W. (ed.) *Ciba Symposium on Immunopotentiation*. London, Elsevier, p. 29.

22. Combined surgery and *Corynebacterium parvum* for treatment of a metastasizing tumour in mice

J. E. CASTRO and TESSA E. SADLER, *Urological Unit, Department of Surgery, Royal Postgraduate Medical School, London*

The effects of *Corynebacterium parvum* on the primary Lewis lung carcinoma and its metastases were studied in female C57/BL mice.

When intravenous or intraperitoneal *C. parvum* was given at the same time as subcutaneous inoculation of tumour there was significant reduction in the primary tumour mass and number of pulmonary metastases detected by the methods described by Wexler (1966). Contralateral subcutaneous *C. parvum* had no effects on either the primary tumour or its metastases.

Pulmonary metastases were not observed 10 days after tumour inoculation, but despite excision of the primary tumour at that time pulmonary metastases were consistently found at 21 days.

The combined effects of surgical excision of the primary tumour at day 10 and intravenous injection of *C. parvum* on pulmonary metastases were studied. When surgery and injection of *C. parvum* were on the same day there was only minimal protection, but if *C. parvum* was given one or more days before tumour excision there was protection; indeed, some mice were permanently cured of tumour.

These results suggest that in defined conditions *C. parvum* can prevent pulmonary metastases from the Lewis tumour and it may be useful adjuvant therapy for tumours that have poor prognosis after surgery alone.

WEXLER H. (1966) Accurate identification of experimental pulmonary metastases. *J. Natl Cancer Inst.* **36**, 641–645.

23. The relationship between gastro-oesophageal sphincter pressure and gastro-intestinal hormone stimulation

C. H. CALVERT, T. G. PARKS and K. D. BUCHANAN, *Departments of Surgery and Medicine, Queen's University, Belfast*

It has been postulated that the basal gastro-oesophageal sphincter pressure is regulated by plasma gastrin concentration (Lipshutz et al., 1972) and that the pressure increase after alkali and protein is due to gastrin release (Castell and Harris, 1970).

Gastro-oesophageal sphincter pressure was monitored in 40 fasting healthy volunteers for 20 minutes before and 2 hours after an alkali, protein or fat meal. Blood samples were taken for gastrin, secretin, total glucagon-like immunoreactivity (GLI) and pancreatic glucagon radio-immunoassays.

Basal sphincter pressures and basal plasma gastrin concentrations did not show any correlation. After alkali, sphincter pressure increased significantly ($P < 0\cdot01$), but plasma gastrin concentration showed no increase. With protein, sphincter pressure increased significantly ($P < 0\cdot01$) and plasma gastrin concentration also increased significantly ($P < 0\cdot001$). However, the gastrin rise occurred in the first hour whereas the pressure rise lasted 2 hours. Sphincter pressure fell significantly with fat ($P < 0\cdot001$), but plasma glucagon and total GLI did not show a significant rise. Secretin concentration fell transiently after protein stimulation.

This study, with the lack of correlation between gastro-oesophageal sphincter pressures and hormone concentrations, both in the basal and stimulated state, does not support the above hypotheses.

CASTELL D. O. and HARRIS L. D. (1970) Hormonal control of gastroesophageal-sphincter strength. *New Engl. J. Med.* **282**, 886–889.

LIPSHUTZ W., HUGHES W. and COHEN S. (1972) The genesis of lower esophageal sphincter pressure: its identification through the use of gastrin antiserum. *J. Clin. Invest.* **51**, 522–529.

24. Observations of gastric mucosal blood flow using ^{99}Tc in rat and man

T. V. TAYLOR, B. R. PULLAN, J. B. ELDER and B. TORRANCE, *Manchester Royal Infirmary*

The standard method for measuring gastric mucosal blood flow (GMBF) experimentally is aminopyrine clearance (Jacobsen et al., 1966). Using the clearance principle and the criteria of Smith (1951) and Pitts (1966) we have compared GMBF in three groups of 8 rats, each receiving one of the following isotopes: (1) ^{14}C-labelled aminopyrine, (2) tritiated quinine or (3) ^{99}Tc. Under halothane anaesthesia the basal flows were: *0·023±0·006, 0·022±0·005* and *0·0196±0·004 ml/min for these* agents respectively.

As ^{99}Tc is non-toxic and gives results comparable to agents used in the experimental animal, a preliminary study has been made in man.

In 10 fasting conscious patients (7 duodenal ulcer, 2 gastric ulcer and 1 Polya gastrectomy) 1 mCi Tc was given intravenously, and gastric secretion and venous blood samples were collected at 15-minute intervals. After four basal collections, pentagastrin (6 µg/kg) was given intramuscularly and collections continued for a further 60 minutes. Aliquots of gastric juice and venous blood were counted in a Panax scintillation counter, and acid output was also determined.

Mean fasting GMBF was 31·6 ml/min for duodenal ulcer patients, 11·4 ml/min for gastric ulcer patients and 3·4 ml/min following a Polya gastrectomy. After pentagastrin the GMBF increased by 100–250 per cent in all the duodenal ulcer patients.

These results suggest that ^{99}Tc is a suitable agent for the measurement of GMBF in the conscious human subject.

JACOBSEN E. D., LINFORD R. H. and GROSSMAN M. I. (1966) Effects of histamine on gastric blood flow in conscious dogs. *Gastroenterology* 51, 466–472.

PITTS R. (1966) *Physiology of the Kidney and Body Fluids.* Chicago, Year Book, p. 64.

SMITH H. (1951) *The Kidney.* Oxford University Press, p. 47.

25. Secretagogue-produced duodenal ulcers in the rat and their prevention by the gastric secretory inhibitor UK 9040

S. N. JOFFE, R. GASKIN, A. A. J. BARROS D'SA, A. A. MELO, R. J. N. GRIBBLE, D. P. GIRVAN and J. H. BARON, *Department of Surgery, Royal Postgraduate Medical School, London*

Animal models of peptic ulcers may help us to understand the natural history and treatment of this disease. Of the various methods used to produce duodenal ulcers in animals, one of the nearest to the clinical situation is the production of gastric hypersecretion by infusing secretagogues (Robert et al., 1971).

In the present study pentagastrin (2 or 4 µg/kg min^{-1}) with carbachol (0·4 or 0·8 µg/kg min^{-1}) were infused subcutaneously into rats for 6–48 hours. In each group of 30 rats the duodenal ulceration was expressed as follows: the 'duodenal ulcer index', which is the sum of one-tenth of the percentage incidence of ulcers; severity of ulcer (graded 0 to 5+); and the number of ulcers per duodenum. With increasing duration of infusion and increasing doses of pentagastrin and carbachol there was an increase in the incidence, severity, number, duodenal ulcer index score, caudad distribution, perforation and deaths from peritonitis. With pentagastrin (4 µg/kg min^{-1}) and carbachol (0·8 µg/kg min^{-1}) for 24 hours, every rat developed a duodenal ulcer of 5+ severity, with a mean of 3 ulcers per animal and a 7 per cent mortality from perforation. Control rats infused with saline did not develop any mucosal changes in the stomach or duodenum.

With this satisfactory duodenal ulcer model the gastric secretory inhibitor, UK 9040, an analogue of the antihistamine triprolidine (Hamer et al., 1972), was given orally, 10–100 mg/kg, 1 hour before and at various times during infusion of the secretagogues. The higher the dose and the more frequent the dosage, the lower was the incidence, severity, number and perforations of duodenal ulcers. For example, 100 mg/kg of UK 9040 before infusion completely inhibited the formation of duodenal ulcers in two-thirds of the rats and the ulcers were fewer and less severe.

HAMER D. B., BARON J. H. and SPENCER J. (1972) Studies with a new gastric secretory inhibitor (UK 9040) in the dog. *Br. J. Surg.* 59, 902.

ROBERT A., STOWE D. F. and NEZAMIS J. E. (1971) Prevention of duodenal ulcers by administration of prostaglandin E 2 (PGE 2). *Scand. J. Gastroenterol.* 6, 303–305.

26. The interpretation of plasma gastrin results—an explanation

R. C. G. RUSSELL, S. R. BLOOM and SHEILA JONES, *Surgical Unit, St Mary's Hospital Medical School, London*

The results of radio-immunoassay of plasma gastrin levels in the basal state vary widely (Hansky and Korman, 1973). Two factors may be responsible: first, different antibodies used by different workers; secondly, the specificity of antibody for big (BG) and little (LG) gastrin. The latter will determine the absolute basal level in that BG predominates in the fasting state and LG in the stimulated phase (Yalow and Berson, 1971).

We report here the cross-reactivity of three antibodies (Gas 8, Gas 9 and RCS 8) for BG and LG, and the values for basal plasma gastrin in 10 normal, 15 duodenal ulcer and 6 post-surgical patients. We have also studied the 6 post-surgical patients after stimulation by a standard meal.

The cross-reactivity for BG was Gas 8, Gas 9, 45 per cent; RCS 8, 68 per cent. Basal plasma gastrin was similar for Gas 8 and 9 but high for RCS 8. The values for incremental response showed no differences. These results suggest that the basal plasma gastrin level is higher the greater the cross-reactivity with BG, and confirms that after a meal the rise is mainly due to LG. Plasma gastrin results cannot be interpreted without knowing the component of gastrin being measured.

Antibody	Normal subjects (pg/ml)	Duodenal ulcer patients (pg/ml)	Meal stimulus Gastrin response (ng)	Meal stimulus Incremental response (ng)
Gas 8	13·7±1·0	18·0±2·0	8·3±1·5	3·8±0·7
Gas 9	13·9±0·6	17·6±1·4	8·1±1·1	3·1±0·5
RCS 8	28·1±3·1	29·6±2·8	12·5±2·1	3·1±0·6

HANSKY J. and KORMAN M. G. (1973) Immunoassay studies in peptic ulcer. *Clin. Gastroenterol.* 2, 275–291.

YALOW R. S. and BERSON S. A. (1971) Further studies on the nature of immunoreactive gastrin in human plasma. *Gastroenterology* 60, 203–214.

27. Salbutamol: effect on acid secretion and plasma gastrin in human subjects

L. P. FIELDING, J. R. KILBORN and R. C. G. RUSSELL, *Surgical Unit, St Mary's Hospital Medical School, London*

Salbutamol, a β_2 adrenergic stimulant, reduces both pentagastrin- and food-stimulated gastric acid secretion in the dog. These changes are similar to those found with metiamide (Fielding et al., 1974). We have studied the effect of salbutamol on acid secretion and plasma gastrin in human volunteers.

Four subjects were studied twice; placebo or salbutamol 8-mg tablets were taken 2 hours before measurement of basal acid output. Pentagastrin infusion (10 µg/kg hr^{-1}) followed for a 2-hour period.

Mean basal acid output was reduced (3·8–1·0 mEq/hr) as was stimulated acid output in the first and second hours (first hour 16·5–5·4 mEq/hr; second hour 18·1–8·9 mEq/hr).

Seven male subjects had an 'English' breakfast test on four occasions twice preceded by a placebo tablet and twice by a salbutamol 4-mg tablet. Blood samples were taken at 15-minute intervals for 3½ hours and plasma gastrin concentrations measured by radio-immunoassay.

The group means ±s.e.m. for basal and peak plasma gastrin concentrations and integrated gastrin response (IGR) were similar.

	Placebo	Salbutamol
Basal plasma gastrin (pg/ml)	15·6±4·1	109±2·1
Peak plasma gastrin (pg/ml)	32·9±3·1	33·5±3·2
IGR (ng/2 hr)	2978·3±347·1	2969·1±325·9

Thus, salbutamol effectively reduces basal and stimulated acid secretion and does not evoke hypergastrinaemia. These results suggest that salbutamol, like metiamide, has an action both on the acid-secreting cell complex and on the antral gastrin-producing cell.

FIELDING L. P., CURWAIN B. P., RUSSELL R. C. G. and BLOOM S. R. (1974) Evidence for separate actions of an adrenergic β_2 stimulant and a histamine H_2 blocker on the oxyntic and gastrin cells. *Br. J. Surg.* 61, 914.

28. The interaction of cholinergic and histaminic blockades on the parietal cell: therapeutic possibilities

M. H. THOMPSON, MARGITTA ALBINUS, E. L. BLAIR, J. D. REED and C. W. VENABLES, *Departments of Physiology and Surgery, University of Newcastle upon Tyne*

The blockade of histamine H_2 receptors offers new possibilities in the treatment of peptic ulcer disease, and although ulcers heal in the majority of cases, we find that not all patients respond completely to this therapy.

The possibility that there exists a cholinergic pathway controlling part of the gastric acid secretory response separate from that controlled by the histamine-sensitive receptors was investigated in conscious gastric fistula cats. This was done by comparing the inhibition produced by two doses each of metiamide and atropine, used separately and in combination, of maximal pentagastrin-stimulated acid secretion.

The results appear in the table.

	No atropine	Atropine 2 μg/kg	Atropine 100 μg/kg
No metiamide		11·5 ±7·8	40·5 ±6·1
Metiamide 1 mg/kg	8·2 ±9·0	30·4 ±3·4	44·4 ±3·8
Metiamide 5 mg/kg	58·5 ±7·1	71·8 ±1·8	90·2 ±2·2

Results are expressed as percentage mean inhibition ±1 s.e.m.; $n = 6$ in each test.

These data suggest that therapeutic combinations of H_2 and anticholinergics might be beneficial in circumstances where the same dose of either agent would be ineffective.

The additive nature of the inhibition produced by the combination of these two drugs suggests that histaminic and cholinergic pathways, at least in the cat, act separately on the parietal cell and do not interact with each other.

29. The effect of haemorrhagic shock upon plasma glucose, insulin and cyclic AMP levels in the pig

K. PRUDHOE, P. D. WRIGHT, A. L. LATNER and I. D. A. JOHNSTON, *Departments of Surgery and Clinical Biochemistry, University of Newcastle upon Tyne*

Glucose intolerance following injury has been recognized for many years. No single hormone has been shown to be responsible for these changes, although it has been suggested that a fall in the availability or activity of insulin might be responsible (Wright et al., 1974). Cyclic AMP is believed to play a part in the release of many hormones from their cells of origin (Robison et al., 1971).

Nine pigs were subjected to an intravenous glucose tolerance test (0·5 g/kg) during haemorrhagic shock (blood pressure 50 mm Hg). Portal and systemic blood was sampled, and plasma glucose, insulin and cyclic AMP estimated.

Hyperglycaemia persisted until 2 hours after glucose loading, with systemic glucose levels significantly greater than portal glucose levels ($P<0·005$). A significant increase in plasma insulin occurred, with portal levels being greater than systemic levels. Similarly, an increase in plasma cyclic AMP levels occurred, with portal levels higher than systemic levels ($P<0·0005$). A highly significant correlation was found between plasma insulin and plasma cyclic AMP levels ($P<0·0005$).

It is believed that the raised portal cyclic AMP levels are a reflection of the pancreatic insulin release during haemorrhagic shock, although it is not possible to exclude the release of hormones such as glucagon within the portal circulation or changes in cell membrane permeability as being responsible for these changes in plasma cyclic AMP.

ROBISON G. A., BUTCHER R. W. and SUTHERLAND E. W. (1971) *Cyclic AMP*. New York, Academic Press.

WRIGHT P. D., HENDERSON K. and JOHNSON I. D. A. (1974) Glucose utilization and insulin secretion during surgery in man. *Br. J. Surg.* 61, 5–8.

30. Changes in plasma cortisol levels during cardio-pulmonary bypass

K. M. TAYLOR, J. V. JONES, M. S. WALKER, L. G. S. RAO and W. H. BAIN, *Cardiac Surgery Unit and Regional Steroid Laboratory, Royal Infirmary, Glasgow*

Plasma cortisol levels were measured before, during and after operation in 12 patients undergoing cardiac surgery. Six patients requiring closed heart procedures exhibited the typical cortisol response to surgical trauma (Franksson and Gemzell, 1954). The other 6 patients underwent open heart procedures using conventional normothermic cardiopulmonary bypass. In the latter group a highly significant reduction in plasma cortisol ($P<0·001$) occurred during extracorporeal circulation (ECC) which cannot be accounted for by the expected dilutional effect of the fluid prime employed in each case.

Tetracosactrin zinc phosphate (Synacthen 0·25 mg i.m.) was administered during bypass in a further 4 patients. In each case there occurred a rise in the plasma cortisol of >200 nmol/l (i.e. a positive response), indicating that in these patients adrenocortical secretion during bypass had been submaximal. This finding contrasts with the previous observations in general surgical patients in whom administration of ACTH during operation produced no further increase in plasma cortisol, suggesting an already maximal response to surgical stress (Hume et al., 1962).

Measurement of the free (non-protein bound) cortisol content in 6 bypass patients indicates that despite the marked fall in total plasma cortisol there is an actual increase in the free cortisol content during the period of bypass.

FRANKSSON C. and GEMZELL C. A. (1954) Blood levels of 17-hydroxycorticosteroids in surgery and allied conditions. *Acta Chir. Scand.* 106, 24–30.

HUME D. M., BELL C. C. and BARTER F. M. (1962) Direct measurement of adrenal secretion during operative trauma and convalescence. *Surgery* 52, 175–187.

31. Direct effect of ethanol on the isolated canine pancreas

J. M. FITZPATRICK, O. FITZGERALD, P. FITZGERALD and K. F. MCGEENEY, *Department of Surgery, University College, Dublin*

Some effects of ethanol on pancreatic function have been found to be mediated through the stomach in whole animals. The response of the secretin-stimulated isolated perfused pancreas to ethanol has been investigated in this study.

Experiments were carried out on the totally isolated perfused pancreas of 8 dogs. The glands were stimulated by a constant infusion of secretin (Boots). In 5 dogs 4 u./hr were infused; in 1 dog each 6, 2 and 1 u./hr were infused. The output of the gland was collected in 10-minute specimens for 3 hours. After the first hour three different concentrations of ethanol were infused for half an hour each.

In 4 dogs ethanol dosages of 50 mg, 100 mg and 1 g/hr were used. In another 4 the dosages were 1, 3 and 10 g/hr. Measurements of volume, amylase, lipase and trypsin output were performed.

At low flow rates (1 μl/min) induced by 1 u. secretin/hr ethanol did not cause secretion. At higher flow rates (above 20 μl/min) induced by 4 or 6 u. secretin/hr ethanol stimulated both volume and enzyme output, and also increased enzyme concentration. These studies indicate that ethanol, even in moderate amounts, can stimulate pancreatic secretion in the ecretin-stimulated gland. This effect, without the mediation of other organs, may be a direct one.

32. Femoropopliteal vein bypass: a new approach to assessing 'run-off'

D. CHARLESWORTH, F. D. CAVE, ANNE WALKER and G. P. NAYLOR, *Departments of Surgery and Medical Physics, University Hospital of South Manchester*

One of the factors which influence the outcome of a femoropopliteal bypass is the outflow or 'run-off' from the lower end of the graft. There are several methods of estimating this but none is reliable. We have measured 'run-off' by calculating mpedance to pulsatile flow.

Simultaneous measurements of pressure and flow were made in the common femoral and popliteal arteries before and after operation in 12 patients. The modulus of impedance in mm Hg/ml min^{-1} over a range of 2–6 Hz was calculated by Fourier analysis of the pressure and flow waves. Preoperatively the mean values for impedance of the superficial femoral and popliteal arteries were 0·43–0·84 and 0·8–1·05 mm Hg/ml min^{-1} respectively. In 9 of the 12 patients the popliteal impedance fell to less than 0·4 mm Hg/ml min^{-1} after reconstruction. There was a significant difference between the pre- and postoperative values at each frequency ($P<0{\cdot}004$). All 9 of these grafts remained patent. In 3 patients popliteal impedance remained high and each graft occluded postoperatively.

Similar results were obtained from measurements of common femoral impedance.

We conclude that input impedance gives a good indication of the capacity of the arterial tree to accept an increased flow and may lead to a useful measure of 'run-off'.

33. The haemostatic effect of ethamsylate (Dicynene) in general surgery

R. S. ARNOT, A. RASHID, MARY EVANS and A. V. POLLOCK, *Scarborough Hospital, Yorkshire*

Ethamsylate has been shown in pigs to be an effective systemic haemostatic agent (Deacock and Birley, 1969), reducing the amount of small vessel haemorrhage produced by a dermatome.

To evaluate this drug in a general surgical practice, blood loss during incisions for 285 major intra-abdominal operations was measured by swab weighing. Approximately half the patients were randomly allocated to receive ethamsylate 750 mg intramuscularly before operation, the remainder being controls.

It soon became apparent that blood loss during incision is dependent primarily on surgical technique and the level of blood pressure. In 49 abdominal incisions (made by a consultant) during which the systolic pressure remained at a level more than 40 mm Hg below the patient's normal pressure ethamsylate reduced bleeding to less than half the control mean ($t=2{\cdot}397$, $P<0{\cdot}05$). However, in 86 patients in whom the incisional pressure was near the preoperative level (and larger vessel bleeding therefore more important) those given ethamsylate did not lose significantly less blood than the controls. In the same trial, patients receiving low dose subcutaneous heparin were shown to lose no more blood during incisions than the controls.

The claim that ethamsylate reduces small vessel bleeding appears to be substantiated.

DEACOCK A. R. DE C. and BIRLEY D. M. (1969) The antihaemorrhagic effect of ethamsylate (Dicynene). *Br. J. Anaesth.* 41, 18–24.

34. Serum, tissue and wound levels of two cephalosporins

B. W. ELLIS, R. C. SPENCER, R. DE L. STANBRIDGE and J. M. SIKORSKI (H. A. F. DUDLEY), *Surgical Unit and Department of Bacteriology, St Mary's Hospital Medical School, London*

Prevention of infection in surgical wounds by the use of systemic antibiotics has a firm experimental and clinical basis. Currently each new antibiotic or combination of agents has to be evaluated by clinical trial which is tedious and may disadvantage a number of the control patients. If an inference about wound concentrations could be made from other data, doses and times of administration might be chosen *a priori* to maximize the effectiveness of any new agent.

We have studied the skin abrasion technique of Raeburn (1971) as a marker for wound concentration of the cephalosporins, cephaloridine and cefazolin. Adult male patients undergoing elective surgery were given 1 g of either cephaloridine or cefazolin with their premedication and 6 and 12 hours thereafter. Blood, exudate and wound drainage concentrations of the antibiotics were determined at intervals during the first 24 postoperative hours. Wound concentrations of antibiotic lagged behind those of blood and the abrasion but more closely approached the latter. Cefazolin wound concentrations were significantly higher than those of cephaloridine.

Simultaneous blood and skin abrasion levels promise to be a rapid and effective means of screening antibiotics for their penetration into wounds and should prove helpful in evaluating proposed dosage regimens of other antibiotics.

RAEBURN J. A. (1971) A method for studying antibiotic concentrations in inflammatory exudate. *J. Clin. Pathol.* 24, 633–635.

35. Serum follicle-stimulating hormone estimation in the investigation of azoospermia

F. J. BRAMBLE, A. L. HOUGHTON and H. S. JACOBS (R. E. WILLIAMS), *The General Infirmary, Leeds, Bradford Royal Infirmary and St Mary's Hospital Medical School, London*

The investigation of azoospermia includes testicular biopsy, usually under general anaesthetic. Patients with a histological picture suggesting obstruction may be amenable to treatment, but those with germ cell aplasia or arrest are at present untreatable.

Franchimont et al. (1972) have observed that when gametogenesis is arrested before spermatid differentiation serum follicle-stimulating hormone (FSH) concentration is raised.

In 18 cases of complete azoospermia we have measured serum FSH and obtained bilateral testicular biopsies. In 13 cases we have evaluated the response of serum FSH to gonadotrophin-releasing hormone (GRH).

All the cases with germ cell arrest prior to spermatid differentiation had elevated basal levels of FSH and an exaggerated response to GRH.

We suggest that it is possible to identify those instances in which testicular biopsy is indicated by estimation of basal serum FSH. The response to GRH may be of diagnostic help in cases with basal FSH concentration at the upper limit of normal. High basal levels of FSH indicate germ cell aplasia or arrest and in these cases a general anaesthetic and testicular biopsy is not helpful and may be avoided.

FRANCHIMONT P., MILLET D., VENDRELY E., LETAWE J., LEGROS J. J. and NETTER A. (1972) Relationship between spermatogenesis and serum gonadotropin levels in azoospermia and aligospermia. *J. Clin. Endocrinol.* 34, 1003–1008.

36. The relationship between spleen size, clinical staging and histological features in breast cancer

J. G. ROBERTS, A. M. MANDER, R. W. FORTT, K. G. LEACH, A. S. BLIGH and M. BAUM, *Departments of Surgery, Pathology, Medical Physics and Diagnostic Radiology, Welsh National School of Medicine and University Hospital of Wales, Cardiff*

Computer analysis of splenic scintigraphs obtained following reinjection of heat-damaged autologous ^{99}Tc^{m}-labelled red cells can accurately assess spleen size (Roberts et al., 1974).

This technique has been used in 60 patients with breast cancer and 6 controls. Cancer patients had significantly larger spleens (138±59 g) than controls (85±32 g; $P<0{\cdot}05$). Early breast cancer patients with tumours greater than 5 cm maximum diameter had spleens significantly larger (153 ± 62 g) than those with tumours less than 5 cm (124 ± 55 g; $P < 0·05$).

Analysis of the 26 patients within whom nodal histology was available showed that patients with involved nodes had larger spleens (147 ± 48 g) than those with negative nodes (109 ± 31 g), but this difference did not reach statistical significance ($0·1 > P > 0·05$).

Tumours were graded histologically into well to moderately differentiated, poorly differentiated and anaplastic. The well to moderately differentiated group had significantly larger spleens (140 ± 67 g) than the control group ($P < 0·05$). The spleens of patients with poorly differentiated tumours were also larger than the controls (146 ± 54g; $P < 0·02$), while patients with anaplastic tumours did not have a significant increase in spleen size (100 ± 35 g).

These results suggest that the splenic component of the host reaction to cancer may be related to tumour volume in all but anaplastic cancers and mirror the behaviour of the reticulo-endothelial system as a whole as judged by the clearance of the colloidal particles (Baum, 1975).

BAUM M. (1975) The effect of administered hormones on the immune reaction. In: STOLL B. A. (ed.) *Immunological Aspects of Breast Cancer*. London, Heinemann. In the press.

ROBERTS J. G., WISBEY M. L., LEACH K. G. and BAUM M. (1974) Spleen size in breast cancer. British Association for Cancer Research Autumn Meeting, Middlesex Hospital, September 1974.

37. Operative mortality and postoperative morbidity of highly selective vagotomy

D. JOHNSTON, *University Department of Surgery, The General Infirmary, Leeds*

Three hundred patients with duodenal ulcer have been treated by highly selective vagotomy (HSV) in Leeds in the past 6 years, without operative mortality. After operation they can be managed without a nasogastric tube or intravenous infusions. However, recent reports of necrosis of the lesser curvature after HSV prompted this survey, in which a questionnaire was sent to surgeons known to be using HSV.

Replies were received from 33 centres: in Europe (19), Scandinavia (10), North America (3) and Australia (1); 4557 patients had undergone elective HSV for duodenal ulcer alone, with 12 deaths (0·26 per cent mortality). Seven of the deaths were due to cardiorespiratory problems or to pulmonary embolism. Seven cases of necrosis of the lesser curve or fundus were reported, with 3 deaths. Approximately half of the surgeons were using HSV for 90 per cent or more of their duodenal ulcer patients, while most of the others were engaged in prospective random trials of HSV. Thirty patients (0·7 per cent) developed gastric retention or ileus in the early post-operative period, but only 5 of these (0·1 per cent) required reoperation. Twenty-nine patients (0·7 per cent) developed persisting gastric stasis several months or years after HSV and most of these patients underwent reoperation.

Necrosis of the upper stomach seems to be a rare but specific complication of HSV. Gastric retention appears to be more frequent after HSV than after vagotomy with drainage. The operative mortality of HSV is less than the reported mortality of vagotomy with drainage (0·8 per cent) or of gastric resection (1–2 per cent).

38. The radio-isotope hepatogram in the diagnosis of jaundice

A. WATSON, D. E. BONE, H. J. TESTA and B. TORRANCE, *Departments of Gastroenterology and Medical Physics, Manchester Royal Infirmary*

The distinction between 'medical' and 'surgical' jaundice is often difficult, owing to the lack of specificity of biochemical liver function tests and difficulty in assessing hepatocellular function and biliary tract patency in the jaundiced patient. A non-invasive isotopic technique which gives reliable information on these parameters and results in a high degree of accuracy in the classification of jaundice is presented.

^{131}I Rose Bengal is administered intravenously, and count rates during hepatic uptake and biliary excretion are recorded over the liver, biliary tract and duodenum using a gamma camera–computer system with an electronic light pencil. Blood clearance is simultaneously measured, and from these data the $T_{\frac{1}{2}}$ of uptake and excretion quotient are determined.

The results of the first 50 examinations show that by qualitative assessment of the uptake and excretory phases of the 'hepatogram', and determination of the $T_{\frac{1}{2}}$ and excretion quotient, jaundice can be classified with a 94 per cent accuracy, often where liver function tests are equivocal or misleading.

It is concluded that this technique enables an accurate classification of jaundice, and by permitting quantitative assessment of hepatocellular function in the jaundiced patient enables this to be studied both during and after recovery from obstructive jaundice.

39. A controlled clinical trial of three methods of perineal wound management following excision of the rectum

T. T. IRVIN and J. C. GOLIGHER, *University Department of Surgery, The General Infirmary, Leeds*

Traditionally, the perineal wound is left open following excision of the rectum. Recently, various methods of primary suture of the perineal wound have been described, and primary wound healing has resulted in a significant proportion of cases (Haxton, 1970; Broader et al., 1974). However, there have been no objective studies of the relative merits of the different methods of perineal wound closure.

Three methods of perineal wound closure were compared in a randomized prospective study of 106 patients undergoing excision of the rectum. In method 1 the perineal wound was partially closed around a corrugated drain. In methods 2 and 3 the wound was closed by primary suture with suprapubic drainage of the presacral space. The pelvic peritoneum was sutured in methods 1 and 2, but not in method 3.

Primary wound healing occurred in 45·2 per cent of patients treated by method 2, and in 42·9 per cent of cases treated by method 3. Operative contamination of the perineal wound had an adverse effect on wound healing ($\chi^2 = 4·50$, $P < 0·05$). The incidence of persistent wound sinuses at 3 and 6 months after primary closure was less than that encountered after open drainage.

It was concluded that primary closure of the perineal wound is the treatment of choice, except in cases in which operative contamination of the perineal wound has occurred.

BROADER J. H., MASSELINK B. A., OATES G. D. and ALEXANDER-WILLIAMS J. (1974) Management of the pelvic space after proctectomy. *Br. J. Surg.* **61**, 94–97.

HAXTON H. (1970) *Surgical Techniques*. Bristol, Wright.

40. The effect of some autonomic receptor agonists and antagonists on motor activity of the human ureter

N. LONGRIGG (I. E. GILLESPIE), *Department of Surgery, Manchester Royal Infirmary*

Smooth muscle of the human upper urinary tract has been shown to possess α adrenoceptors, β adrenoceptors and muscarinic receptors (Longrigg, 1974a, b). The present study was designed to test the effect of drugs which may hence theoretically be expected to modify ureteral activity in the clinical situation.

Phasic intra-ureteral pressure changes accompanying peristalsis were recorded in 57 female patients by the use of indwelling non-occlusive open-ended fluid-filled catheters. Drug effects were studied in 23 of these patients after pre-liminary control periods of 30 minutes.

Atropine (7 patients, 10 ureters) was without any observable effect upon basal pressure, frequency, form, amplitude or rhythm of the recorded contractions when studied for post-injection periods of 20 minutes. A similar complete absence of effect was noted after propantheline (6 patients, 10 ureters).

Isoprenaline (5 patients, 7 ureters) effected in all subjects a marked decrease in the amplitude of the contraction waves. This depressant effect was maintained throughout the infusion and for approximately 2–5 minutes following termination of the infusion.

Phentolamine (5 patients, 8 ureters) effected a marked decrease in the frequency of contraction, a slight fall in basal pressure and an increase in duration of the contraction waves. Such changes persisted for a minimum of 6 minutes after which there was a return towards control values.

These results clearly indicate the inhibitory effects of isoprenaline and phentolamine on the motor activity of the human ureter. Their effects upon the abnormally hyperactive ureter remain to be investigated.

LONGRIGG N. (1974a) Autonomic innervation of the renal calyces. *Br. J. Urol.* 43, 317–370.

LONGRIGG N. (1974b) Experimental and clinical studies on the renal calyces, pelvis and ureter. M.D. Thesis, University of Manchester.

41. The Doppler scan and deep vein thrombosis

P. FISH, V. V. KAKKAR and T. K. DAY, *Departments of Medical Physics and Surgery, King's College Hospital Medical School, London*

The ultrasonic technique is a quick and simple way of detecting complete occlusion of the popliteal, femoral or iliac veins. It is less reliable, however, in demonstrating extensive early thrombi which often propagate along the veins without producing any significant obstruction. Furthermore, flow in large collaterals or in a very large superficial vein cannot be distinguished from that in the main deep veins and a false negative result is produced. To overcome these disadvantages a new imaging system has been developed using ultrasound, and is described together with the results of its clinical use.

In this new technique a picture of an internal cross-section of a blood vessel is built up on the cathode-ray tube by moving the transducer probe backwards and forwards across the skin surface, so that the ultrasonic beam sweeps across the vessel of interest. Fifty limbs of 41 surgical patients with clinically suspected deep vein thrombosis were examined by Doppler scanning and by phlebography. Thirty of 32 (94 per cent) partially and/or totally occluding thrombi in the popliteal and femoral veins were detected by Doppler scan. There was 1 false positive result and 2 false negative results, the overall level of agreement for positive and negative results being 47/50 (94 per cent).

The Doppler scan provides a suitable alternative to phlebography for confirming the presence of clinically suspected deep vein thrombosis.

42. Metabolic abnormalities in tumour-bearing animals

K. C. CALMAN and R. A. MCALLISTER, *Departments of Oncology and Surgery, Western Infirmary, Glasgow*

The metabolism of non-involved organs of tumour-bearing animals has received little attention, though the potential importance of this in relation to the pathogenesis of cachexia is great. We have studied intermediary metabolism in animals bearing a transplantable tumour (the TLX5 lymphoma) and measured both co-enzyme A levels and energy metabolites in liver and muscle 7 days after transplantation of tumour.

The co-enzyme A levels in the liver of tumour-bearing animals is reduced by 78 per cent ($P<0.001$) and in muscle by 37 per cent ($P<0.05$) when compared with the content in control livers. Similarly, there is a reduction in the energy content of such livers (ATP, ADP, AMP) of 59 per cent ($P<0.001$) when compared with controls.

These figures suggest that in the presence of a tumour the intermediary metabolism in liver and muscle is grossly abnormal. Because of the central role of these metabolites in fat, carbohydrate and protein metabolism, the reductions demonstrated may account for several of the metabolic effects of tumours. Current research is aimed at defining the mechanism of this depression and its relationship to cachexia.

43. The role of prolactin in hypercalcaemia

K. K. MAHAJAN, C. J. ROBINSON and D. F. HORROBIN (I. D. A. JOHNSTON), *Departments of Surgery and Physiology, University of Newcastle upon Tyne*

Hypercalcaemia and hypercalciuria is a significant clinical problem in patients with advanced breast cancer (Galasko, 1972). Prolactin suppression in patients with bony metastases and possible hypercalcaemia is followed by relief of bone pain (Stoll, 1972).

We postulate that prolactin plays a role in these changes. A study was therefore planned to investigate the effect of infusion of prolactin on calcium metabolism in intact male Wistar rats and in animals after parathyroidectomy and thyroparathyroidectomy.

Ovine prolactin (10 μg/hr) was infused intravenously for 18 hours in the experimental animals; the control group received the vehicle alone. Urine was collected throughout the infusion period and blood was collected by cardiac puncture at the end of the experiment. Urine and plasma calcium estimations were done by flame photometry.

Three groups of animals were studied: (*a*) intact animals (18 pairs), (*b*) parathyroidectomized animals (7 pairs), (*c*) thyroparathyroidectomized animals (13 pairs), receiving appropriate parathyroid and thyroid hormone replacement.

Prolactin caused a significant hypercalcaemia in all three groups and significant hypercalciuria ($P<0.05$) in the intact and thyroparathyroidectomized groups.

Plasma calcium (mg/100 ml)

Intact		PTX		TPTX	
Control	Exp.	Control	Exp.	Control	Exp.
10·22 ±0·39	10·72 ±0·31	4·9 ±0·22	6·06 ±0·66	8·60 ±0·64	9·90 ±0·21
$P<0.025$		$P<0.05$		$P<0.025$	

PTX, Parathyroidectomized. TPTX, Thyroparathyroidectomized animals. Exp., Experimental.

It is concluded that sustained increased levels of prolactin produce hypercalcaemia and hypercalciuria in rats. These findings support the hypothesis that prolactin may be a factor in the hypercalcaemia of malignancies.

GALASKO C. S. B. (1972) Skeletal metastases and mammary cancer. *Ann. R. Coll. Surg. Engl.* 50, 3–28.

STOLL B. A. (1972) Brain catecholamines and breast cancer: a hypothesis. *Lancet* 1, 431.

44. Cholelithiasis—a metabolic consequence of ileostomy

W. S. J. MAIR, G. L. HILL and J. C. GOLIGHER, *University Department of Surgery, The General Infirmary, Leeds*

A clinical and radiological survey of the incidence of cholelithiasis in 106 ileostomy patients was undertaken and the findings compared with the expected incidence calculated from three large scale necropsy series. Twenty-six patients were found to have gallstones (24·5 per cent) compared with an expected number of between 7·6 and 9·5, the difference being statistically highly significant. The male : female incidence ratio was similar to that found in the necropsy series. Eight out of 47 patients under 40 years of age (17·0 per cent) and 18 out of 59 patients over this age (30·6 per cent) had gallstones, the expected incidences being 2·1 and 13·4 per cent respectively.

Patients with an ileal resection of more than 10 cm, whether the primary condition was Crohn's disease or ulcerative colitis, and Crohn's disease patients with a resection of less than 10 cm showed a significantly increased incidence of cholelithiasis; between three and seven times the expected figures. The incidence in ulcerative colitis patients with an ileal resection of less than 10 cm was not significantly increased.

It is suggested that the difference in incidence between Crohn's disease and ulcerative colitis patients with minimal ileal resection may be due to asymptomatic residual or recurrent lesions in the former condition. The importance of preservation of the terminal ileum at proctocolectomy for ulcerative colitis is emphasized.

45. Adjuvant intravesical thiotepa and bladder tumour recurrence

P. J. R. BOYD and K. G. BURNAND (C. JAMIESON), *St Thomas's Hospital, London*

The anatomical sites of mucosal primary and recurrent transitional cell bladder tumours have been studied prospectively in 32 patients. Primary tumours were found on the base and walls in 30 patients and on the vault in only 2 patients. All the patients were treated endoscopically and were followed up for between 2 and 5 years. During this period 31 patients developed recurrent tumour. In 29 patients the vault was at some stage involved by recurrent tumour. In 7 patients recurrences were limited to the vault.

We suggest that the high proportion of vault recurrence results from implantation of tumour cells at the time of cystodiathermy. In an attempt to reduce the incidence of recurrent tumour a further group of 19 comparable patients was prospectively treated with single dose intravesical thiotepa on completion of cystodiathermy.

In this group 11 patients have developed recurrent tumour but in none of these patients was the vault alone involved. Eight patients remained entirely free of tumour.

The significance of these findings suggests that adjuvant intravesical thiotepa reduces tumour recurrence, possibly by the prevention of cellular implantation.

46. Surgery, the contraceptive pill and postoperative deep vein thrombosis

V. V. KAKKAR, A. F. HIGGINS, S. SAGAR and T. K. DAY, *Department of Surgery, King's College Hospital Medical School, London*

A causal relationship between the use of oral contraceptives and deep vein thrombosis (DVT) occurring in previously healthy women has now been established (Royal College of General Practitioners, 1967). It remains to be determined whether (*a*) conditions known to predispose to thromboembolic disease (such as surgical operation) greatly increase this risk and (*b*) any blood test can be used to identify before surgery the patients likely to develop this complication.

Thirty-seven patients undergoing abdominal surgery were investigated and the ^{125}I-fibrinogen test used to determine the incidence of DVT. Frequent blood samples were withdrawn before, during and after surgery to determine the levels in the inhibitor to activated Factor X (Anti-Xa), a protein moiety thought to play a key part in the coagulation process. Six of 22 patients (27 per cent) on the pill developed DVT, but none of the 15 patients not taking the pill did so; this difference is statistically significant ($P < 0{\cdot}05$). All the patients on the pill had low Anti-Xa levels before surgery as compared with those not taking the pill, and levels were further reduced during surgery in those who developed DVT.

These preliminary findings suggest that the use of the contraceptive pill increases the risk of DVT in patients undergoing surgery and that abnormally low Anti-Xa levels before surgery may identify these 'high risk' patients.

ROYAL COLLEGE OF GENERAL PRACTITIONERS (1967) Oral contraception ana thromboembolic disease. *J. R. Coll. Gen. Pract.* **13**, 267–279.

47. Emotional distress in patients attending a breast clinic

E. C. G. LEE and G. P. MAGUIRE (H. A. F. DUDLEY), *Nuffield Department of Surgery and Department of Psychiatry, University of Oxford, Radcliffe Infirmary, Oxford*

Four hundred women referred to the Breast Clinic of the Department of Surgery completed the Spielberger Stait anxiety and Zung depression scales. Before attending the clinic these women were significantly more anxious than were women attending general surgical clinics. Forty-five per cent of the breast clinic group had abnormal scores compared with 18 per cent of a control group. Although there was a significant drop in anxiety after attending the clinic, those being admitted for biopsy and those diagnosed clinically as having cancer improved least. The same group showed a significant lack of improvement in their depression scales before and after attending the clinic.

At the clinic the communication between surgeon and patient was monitored by independent observers. There was a striking discrepancy between the level of distress detected by the mood scales and that indicated verbally by the women to the surgeon. Sixty-nine per cent of the patients exhibited non-verbal signs of distress which were usually ignored by the surgeon. Subsequent home interviews of the patients and their husbands showed that a significant proportion of these women remained very distressed until the time of operation.

When reassessed 3 months after operation 34 per cent of the cancer patients were still reporting moderate or marked degrees of anxiety or depression compared with 7 per cent in the control group. Although in the patients so far studied there has been an improvement in these parameters at the end of 1 year, there has been an increasing incidence of marital discord, sexual problems and a diminution in leisure and social activities. Similar disturbances have been found in their husbands.

48. The thymic hormone and cellular immunity

G. W. ODLING-SMEE, J. G. CAMBLIN and A. D. ROY, *Department of Surgery, Queen's University, Belfast*

Evidence has accumulated that the thymus produces a humoral agent which has the ability to promote a lymphocytosis in thymectomized animals. This material has been shown to change uncommitted lymphocytes into T cells.

In this experiment a bovine thymus extract was prepared by ammonium sulphate precipitation and gel column separation. This purified extract was used to promote *in vitro* lymphocyte cytotoxicity from patients with osteosarcoma towards their own tumour cells, and of normal lymphocytes against a chemically induced rodent fibrosarcoma. The amount of preincorporated isotope tracer, ^{125}I-iodo-desoxyuridine, released from the tumour cells during the period of the reaction was detected and compared with that when cyclophosphamide, PHA or liver extract was added to the culture medium. An attempt was also made to determine the molecular weight and the amino-acid content of the active agent, thymosin.

The results revealed that there was only minimal unstimulated cytotoxicity against both tumour types. The addition of thymosin to the culture medium produced significantly more cell deaths than when cyclophosphamide, PHA or liver extract was added to the medium. Preliminary *in vivo* studies suggest that injections of thymosin may delay the onset and reduce the incidence of chemically induced tumours.

49. Salbutamol: inhibition of gastric ulceration in the rat

L. P. FIELDING, M. ROUTER and B. P. CURWAIN (H. A. F. DUDLEY), *Surgical Unit and Department of Physiology, St Mary's Hospital Medical School, London*

Induction of acute gastric ulceration in the rat with indomethacin is a widely used technique for the initial study of drugs which may be useful in the treatment of peptic ulceration (Robert et al., 1968). We have studied the effect of the β_2 adrenergic stimulant, salbutamol, on the occurrence of such gastric ulcers.

After 24 hours' starvation, rats were divided into four groups. Normal saline or salbutamol was injected subcutaneously at 0, 120 and 240 minutes; normal saline or indomethacin was injected at 15 minutes, according to the schedule shown in the table. The rats were killed at 300 minutes. Each stomach was fixed in a mixture of formaldehyde and alcohol, then opened and photographed. These photographs were enlarged by projection and the length of each ulcer was measured. The total length of ulceration is recorded in the table.

	Group			
	I ($n = 10$)	II ($n = 16$)	III ($n = 10$)	IV ($n = 12$)
Injection at 0, 120 and 240 min	Saline 0·5 ml	Saline 0·5 ml	Salbu. 2 mg/ 100 g	Salbu. 0·02 mg/ 100 g
Injection at 15 min	Saline	Indo. 2·5 mg/ 100 g	Indo. 2·5 mg/ 100 g	Indo. 2·5 mg/ 100 g
Mean length of ulceration ± s.e.m. (mm)	0	21·2 ± 5·2	0	5·7 ± 1·9

Salbu. = salbutamol. Indo. = indomethacin.
Comparisons (Mann–Whitney *U*-test): Groups II and III, $P<0{\cdot}002$; Groups II and IV, $P<0{\cdot}02$.

Salbutamol protected the animals from developing peptic ulceration; the higher dose afforded complete protection while the lower dose greatly reduced the degree of ulceration.

It is concluded that salbutamol should be evaluated for its role in the treatment of peptic ulcer in man.

ROBERT A., NEZAMIS J. E. and PHILLIPS J. P. (1968) Effect of prostaglandin E_1 on gastric secretion and ulcer formation in the rat. *Gastroenterology* **55**, 481–487.

50. Low dose heparin prophylaxis against pulmonary embolism

S. SAGAR and M. M. KOSHI (V. V. KAKKAR), *North Staffordshire Hospital Centre, Stoke-on-Trent*

The established fact that low dose heparinization is an effective prophylaxis against postoperative deep vein thrombosis (Sharnoff and DeBlasio, 1970; Kakkar et al., 1972) in 'high risk' patients leads inevitably to the question—Is this prophylaxis also effective in reducing postoperative mortality due to fatal pulmonary embolism? A prospective randomized controlled trial was carried out at the North Staffordshire Hospital Centre, Stoke-on-Trent, during the 12-month period April 1973 to March 1974 to study the efficacy of low dose heparin prophylaxis against fatal pulmonary embolism. Five hundred patients over the age of 50 years undergoing elective major surgery were included, of whom 252 received perioperative heparin. Two thoracic, one urological and five general surgeons took part in the trial. In 60 of the 66 patients who died post-mortems were performed by independent consultant pathologists who did not know whether or not the patient had received heparin. None of the heparinized patients died of fatal pulmonary embolism but 8 of the 240 control patients died from this condition. These findings are statistically significant ($P<0{\cdot}05$ with Yates's correction).

There was no evidence from coagulation studies, wound drainage charts or blood transfusion requirements that low dose heparin increased the risk of operative or postoperative bleeding or of wound haematoma formation. Our conclusions are that low dose heparin prophylaxis should be used in all 'high risk' patients undergoing major thoracic, abdominal or urological surgery.

KAKKAR V. V., CORRIGAN T., SPINDLER J., FOSSARD D. P., FLUTE P. T., CRELLIN R. Q., WESSLER S. and YIN E. T. (1972) Efficacy of low doses of heparin in prevention of deep-vein thrombosis after major surgery. A double-blind, randomized trial. *Lancet* **2**, 101–106.

SHARNOFF J. G. and DEBLASIO G. (1970) Prevention of fatal postoperative thromboembolism by heparin prophylaxis. *Lancet* **2**, 1006–1007.

51. Non-invasive investigation for carotid arterial disease by comparison of the characteristics of the supra-orbital and upper limb arterial pulses

M. DE BURGH (H. H. G. EASTCOTT), *Flow Laboratory, St Mary's Hospital, London*

The presence of obstruction or non-laminar flow at the carotid bifurcation might be expected to alter the arrival and form of the supra-orbital pulse wave. We have used mercury strain gauges on the supra-orbital notch and forearm linked to a chart recorder running at 100 mm/sec to ascertain if the diseased bifurcation is detectable. Two variables were studied: the difference between time of arrival of the wave (LAG) and the difference in wave rise time (DRT). Vessels were classified arteriographically as normal (56), partly obstructed (less than 70 per cent of diameter, 46) and obstructed (more than 70 per cent, 18). Both LAG and DRT discriminated between all groups with *P* values of less than 0·001 (Student's *t*-test). Normal distribution of the data permitted application of tolerance limits with confidence probabilities; these indicate that, accepting a 5 per cent error of the second kind, normal is distinguishable from obstruction by LAG with a 5 per cent probability of a false positive and a 25 per cent chance of a false negative or vice versa. Similarly DRT separates partly obstructed from normal with a 10 per cent probability of both a false negative and a false positive diagnosis.

The test is simple and easy to apply, the tolerance limits are acceptable for initial screening and DRT has the particular advantage of detecting minimal disease which may be a source of athero-emboli (Atik et al., 1973).

ATIK M., DEIN I. O. and WOLFSEN N. J. (1973) The significance of ulcerated lesions of the carotid arteries. *Am. Surg.* **39**, 681–687.

52. Radiation dosage in mammography

D. L. ASBURY and P. G. BARKER (R. A. SELLWOOD), *University Hospital of South Manchester*

The feasibility of providing a screening programme for the early detection of carcinoma of the breast depends partly on the dose of radiation applied at mammography. In this study mammography was carried out in 150 women by means of a Watson Mammostand with molybdenum targets of 0·8 and 2·0 mm size. Radiation dosage was recorded by the lithium fluoride thermo-luminescent method and the following principles were defined:

1. The dose of radiation was greatest in the upper inner quadrant.
2. It was greater for the mediolateral view than the craniocaudad.
3. There was no detectable dose to the gonads.
4. The dose was significantly greater in young women.
5. Compression of the breast reduced the dose by up to 50 per cent.

Different film and film–screen combinations were assessed. The latter were vacuum-packed. The following total doses to the upper-inner quadrant were recorded:

Kodak industrial quality film	4·9 R
Agfa-Gevaert-Medichrome film with Kodak screen	1·1 R
Agfa-Gevaert Medichrome film with Ilford screen	0·5 R
3M Trimax XD film and Trimax Alpha-4 screen	0·18 R

A 97 per cent reduction in the dose of radiation was achieved from a mean of 4·9–0·18 R.

53. The effect of highly selective vagotomy and truncal vagotomy with pyloroplasty on gastric emptying of solid food in man

H. J. SHEINER, H. L. DUTHIE, D. C. BARBER and P. J. HOWLETT, *Departments of Surgery and Medical Physics, Sheffield Royal Infirmary*

This study was undertaken to assess the theoretical advantage of highly selective vagotomy (HSV) over truncal vagotomy with pyloroplasty (TV) in maintaining better control of gastric emptying (Johnston and Wilkinson, 1970). Twenty-eight male patients with uncomplicated duodenal ulceration requiring surgery were randomly selected to have either a HSV (14) or TV (14). Gastric emptying studies were carried out using a gamma camera and ^{113m}In–DTPA-labelled solid meal.

One week postoperatively the half emptying time ($T_{\frac{1}{2}}$) was considerably longer for HSV ($P<0{\cdot}005$) and TV ($P<0{\cdot}005$)

groups compared with that before operation (48·5 minutes) or normal subjects (53·0 minutes). By 1 month gastric emptying was still delayed in the TV patients ($P<0{\cdot}01$) compared with normal but not in the HSV group. At 6 months postoperatively the emptying times of both groups had decreased (HSV, 53·2 minutes; TV, 72·0 minutes), but there was no significant difference between operations.

The pattern of emptying was determined by the technique of principal component factor analysis. At 1 month both HSV ($P<0{\cdot}1$) and TV ($P<0{\cdot}05$) differed from preoperative patterns without a significant difference between the two groups. By 6 months the pattern of both HSV and TV groups was similar to preoperative and control patterns.

JOHNSTON D. and WILKINSON A. R. (1970) Highly selective vagotomy without a drainage procedure in the treatment of duodenal ulcer. *Br. J. Surg.* 57, 289–296.

54. Insulin response to carbohydrate infusions in surgical patients

B. J. ROWLANDS, A. E. B. GIDDINGS and R. G. CLARK, *University Surgical Unit, Northern General Hospital, Sheffield*

Intravenous fructose and sorbitol may be used as an alternative to glucose in supplying calories. They have a theoretical advantage of being more rapidly metabolized and are said to be utilized independently of insulin (Miller et al., 1952; Lee et al., 1972). This could be beneficial in postoperative management. This study defines the insulin and glucose responses to carbohydrate infusion in surgical patients.

Three groups of male surgical patients received a 2-hour infusion of 30 per cent carbohydrate solution (glucose, fructose, sorbitol) pre- and postoperatively in a therapeutic dosage. Preoperatively there was no significant rise in plasma glucose or plasma immunoreactive insulin (IRI) during fructose or sorbitol infusion. Basal plasma glucose and plasma IRI levels were significantly raised in all groups postoperatively ($P<0{\cdot}01$ and $P<0{\cdot}001$ respectively). Fructose and sorbitol groups showed a significant rise in plasma glucose ($P<0{\cdot}005$) and a highly significant rise in plasma IRI ($P<0{\cdot}001$) at the end of the postoperative infusion. Fructose and sorbitol tolerance were unchanged.

Following operation both fructose and sorbitol produce an insulin response that was not previously evident. This may indicate a postoperative change in the sensitivity of pancreatic islet cells or in insulin metabolism.

LEE H. A., MORGAN A. G., WALDRAM R. and BENNETT J. (1972) Sorbitol: some aspects of its metabolism and role as an intravenous nutrient. In: WILKINSON A. W. (ed.) *Parenteral Nutrition*. Edinburgh, Churchill Livingstone, pp. 121–137.

MILLER M., DRUCKER W. R., OWENS J. W., CRAIG J. W. and WOODWARD H. (1952) Metabolism of intravenous fructose and glucose in normal and diabetic subjects. *J. Clin. Invest.* 31, 115–125.

55. Steroid and protease inhibition in refractory shock

J. A. R. SMITH, J. N. NORMAN and G. SMITH, *Department of Surgery, University of Aberdeen*

Refractory shock is not common, its nature is obscure and its prognosis poor. Aggressive conventional treatment fails to improve the situation, and pharmacological doses of steroids are popular as therapy. Alternatively, protease inhibitors have been advocated but their use is controversial. Therefore it seemed desirable to compare the use of these agents in refractory shock, using a standard canine shock model.

Refractory shock was induced in four groups by bleeding into a reservoir and maintaining the mean aortic pressure at 40 mm Hg for 2 hours before reinfusion (Wiggers et al., 1948). Methyl prednisolone 30 mg/kg i.v. was given to one group at the time of bleeding, and to another 1 hour later. Aprotinin (Trasylol) 30 000 K.i.u./kg stat. and 10 000 K.i.u./kg hr^{-1} i.v. thereafter was similarly administered to the remaining groups.

When administered before the induction of shock Trasylol maintained cardiac output at a higher level ($P<0{\cdot}005$) and total peripheral resistance at a lower level ($P<0{\cdot}005$) than in the steroid or untreated groups, with improved oxygen availability ($P<0{\cdot}025$) and repayment of oxygen debt. When given after 1 hour of hypotension Trasylol did not affect these parameters.

Methyl prednisolone at the induction of hypotension had a similar but less significant effect on these parameters than Trasylol. Used after 1 hour of shock it increased cardiac output ($P<0{\cdot}01$), oxygen availability, repayment of debt and reduced both total peripheral resistance and the increase in arterial lactate.

Trasylol is therefore effective in ameliorating the situation if given before the development of shock, while methyl prednisolone effectively improves the developed shock state. It is suggested that this may be related to the different modes of action of these drugs.

WIGGERS H. C., INGRAHAM R. C., ROEMHILD F. and GOLDBERG H. (1948) Vasoconstriction and development of irreversible hemorrhagic shock. *Am. J. Physiol.* 153, 511–522.

56. Selective denervation in the treatment of paralytic scoliosis based on electromyographic studies of erector spinae and quadratus lumborum

D. H. R. JENKINS, *University Hospital of Wales, Cardiff*

Electromyographic (EMG) studies were performed on the paraspinal and lateral trunk flexor muscles in 40 children with paralytic scoliosis. Clinical assessment of the activity of erector spinae showed a low correlation with EMG findings. A high degree of correlation was found in quadratus lumborum.

Three distinct patterns of electrical activity and muscle function were observed in patients in whom clinical examination suggested only one main paralytic pattern.

The procedure of selective denervation of particular muscle groups was developed on the basis of the electromyographic findings and one such case was described and illustrated.

Br. J. Surg. Vol. 62 (1975) 165–168

Reviews and notices of books

The Ductus Arteriosus

Donald E. Cassels, MD, Chicago. 235×160 mm. Pp. 345+x, with 143 illustrations. 1973. Springfield, Ill.: Charles C. Thomas. $17.75.

THIS monograph on the ductus arteriosus is written by the Professor of Paediatric Cardiology at the University of Chicago and is clearly addressed to other paediatricians, for there is scant reference to persistent patency in the adult. In the 'developed' world concentration on the problems during childhood may well be justified as most clinicians follow the author's recommendation that a persistent duct should be closed surgically before the child goes to school unless there is some specific contra-indication, and consequently there are very few adolescents or adults with persistent patency in the population.

It is a pity that there is no chapter on the problems associated with surgical treatment, but the surgeon will glean valuable scraps of helpful information by reading this book.

Throughout the book there is extensive reference to the literature, but the reviewer wishes that the author had more frequently summarized this and expressed his own opinion.

Many of the illustrations are excellent, especially the line drawings, but some of the photographs would be more quickly understood if the structures were labelled with initials. The reader would have been saved some justifiable irritation if more care had been taken to present the illustrations correctly. For example, Fig. 118 is upside down, Fig. 121 is apparently absent but in fact appears as Plate 1 at the beginning of the book, Figs. 135, 134 and 133 are presented in that order whereas the text refers to them in numerical order and, most confusing of all, Fig. 137 should appear as Fig. 138 and vice versa in order that the captions may apply to the correct figures.

Following an introduction and a statement on the problem of persistent patency there are interesting chapters on the history, embryology and histology of the ductus arteriosus. Subsequently the anatomy is clearly described, although the statement on p. 61 that the ductus may open into an aneurysmal dilatation at the point of junction with either the pulmonary artery or aorta might be amplified by stating that there is always a fusiform dilatation of the aorta at the site of attachment of the duct except in small children.

Following a short chapter on innervation of the duct, the various theories of closure which have been promulgated are described, but Professor Cassels does not express his own views. Chapter 10 is entitled The Patent Ductus Arteriosus, and there are some who would argue that 'Persistent' would be preferable to 'Patent' as a ductus is, by definition, patent. This chapter includes a quotation from Gibson (Edinburgh) on the criteria required for the diagnosis of patency 'which have not been improved upon'. Figure 40 depicting the various conditions which may simulate a persistent duct and which have to be considered in the differential diagnosis is most useful (the only omission is an arteriovenous fistula between the internal mammary vessels which the reviewer has experienced on one occasion).

There is a lucid chapter on haemodynamics which includes reference to the forward flow in the aortic arch in diastole as well as in systole, and the suggestion is made that this may rob the coronary arteries of their normal flow, a phenomenon referred to as 'coronary steal'. This chapter is followed by a detailed description of the various forms of coarctation which may be found in association with a ductus. Subsequently pulmonary hypertension in association with persistent patency of the duct is discussed in detail, and the indications for surgical closure of the duct in patients with a raised pulmonary vascular resistance are stated on p. 200, but it would have been helpful to surgeons if the indications had been discussed in greater depth.

There is much of interest in the chapters which follow but space does not permit critical review of the subjects covered except to comment that petechiae in subacute bacterial endocarditis are no longer considered by cardiologists to result from arterial emboli. Hence, their appearance in cases of infection of the duct does not necessarily indicate dissemination of emboli via the aorta as stated in the chapter on pathology.

Undoubtedly all paediatric cardiologists should read this book, which, by present day standards, is reasonably priced.

O. S. TUBBS

Clinical Cardiac Radiology

Keith Jefferson, London, and Simon Rees, London. 286×222 mm. Pp. 314+xi, with 377 illustrations. 1973. London: The Butterworth Group. £15.

THIS excellent work succeeds in its intention as a practical book for radiologists and for physicians and surgeons who use the chest radiograph as part of the clinical examination. The book is divided into two parts. The first part consists of a description of the general radiology of the heart and of other systems in heart disease. The second half considers cardiac lesions in clinical groups. There is in the first half a very good description of bone changes in heart disease based on the St Cyres Lecture given by Jefferson in 1971. The material for the book is based on 1500 cases in whom the anatomy and physiology are known from the National Heart Hospital, London, and the clinical practice at that hospital to some extent influences the bias of the book. The congenital heart lesions are mainly in older children and there is little neonatal cardiology. A computer analysis of the material is given in an appendix, and conclusions drawn from this are less helpful than might be expected. The book is very well written, concise and easy to follow. The quality of the 377 illustrations is first class. There is very good correlation of the plain radiograph with the angiogram, and they are both related to the clinical presentation. Barium swallow examination, now not practised as a routine, is perhaps neglected in the description of many of the congenital heart lesions, where it might, in fact, be helpful. The book is, however, to be recommended highly to both radiologist and clinician, for it contains a wealth of material of value to both.

I. H. KERR

Tumours of the Male Genital System

F. K. Mostofi and Edward B. Price, Washington. 260×200 mm. Pp. 310+xiv, with 295 illustrations. 1973. Washington: Armed Forces Institute of Pathology. $8.

TWENTY-ONE years ago the US Armed Forces Institute of Pathology gave us their first fascicle on tumours of the genito-urinary system. It was profusely illustrated, and its excellent text was based on the huge material gathered at the Walter Reed Hospital and the Institute of Pathology. 'Dixon and Moore' became the standard and hallmark of North American pathology, and was to be found on the workbench of pathologists dealing with genito-urinary specimens the world over. Pathologists will not need any review to make them buy this new edition—but what about surgeons? What is in it for them?

The surgeon likely to operate on the prostate, testicle, urethra or penis is bound to find this work useful and interesting. If he works in Britain the most illuminating chapters will be those on the testis and the prostate, his colleagues in Africa may well find the chapters on the urethra and penis more immediately useful. All will have occasion to refer to the work when confronted with problems in any of these organs.

The account of testicular tumours will concern many of us most deeply, since we simply do not know what is best for the young man who presents with a tumour which is not a seminoma.

Our colleagues in North America vie with each other to produce more and more astonishing statistics in favour of radical retroperitoneal node dissection; radiotherapists in the United Kingdom produce even better figures for one group of teratomas, but not for the others. When we try to compare British statistics with those from North America we are entirely frustrated by the impossibility of translating the 'Dixon and Moore' system into the British Testicular Tumour Panel classification ('Collins and Pugh'). Nor do we find anything more accurate in the Dixon and Moore system, as a means of determining prognosis, than the classification of Collins and Pugh, whose distinction between undifferentiated and intermediate teratomas clearly marks out the sheep from the goats. Alas, Mostofi and Price make the comparison no easier, and the simple surgeon who wants to know when (if ever) he ought to do a node dissection on a given patient is as lost as ever.

As for the prostate, Mostofi and Price give a fascinating account of benign and malignant change in the gland in a section full of experience and wisdom, but it was odd to find them claiming value for histological grading in prostatic cancer, when Mostofi and Byar have just stated that any given prostatic cancer will display the entire spectrum of tumour grades if it is examined carefully by the step-section technique. What is the poor old surgeon to believe, and what ought he to do when confronted by the patient from whom he has just obtained a fragment of tissue with a needle biopsy?

Few of us see many disorders of the urethra, seminal vesicles or penis, but when we do, this is surely one of the most illuminating works of reference we can consult. It is richly illustrated with many fine colour plates, and it is unbelievably cheap by present day standards. Indeed, such a fine book deserves a better binding, and it would still be a bargain if one had those cruel staples taken out and the work rebound in a manner more suited to its quality.

JOHN BLANDY

Blood Compatible Synthetic Polymers

Stephen D. Bruck, Maryland. 235 × 160 mm. Pp. 131 + x, with 68 illustrations. 1973. Springfield Ill.: Charles C. Thomas. $9.75.

In this day of increasing specialization it is a delight to see a book written especially to bridge one of the 'gaps'. The book is divided into three sections: (1) the chemistry of polymers; (2) basic physiology of blood; (3) the problems of blood and polymer interaction. Each part is dealt with clearly and concisely and the whole is extremely readable. For its small size the book is comprehensive and should be particularly suitable for polymer scientists wishing to understand the basic biological problems and for medical practitioners wishing to have an improved knowledge of the many diffculties with synthetic polymers in use in medical practice today. It is this latter group who I think will find it particularly useful for background understanding. However, as this book sits so firmly astride two differing disciplines it may well be largely ignored by the two groups and not reach the audience it deserves. At approximately £4 it is expensive but nevertheless a well worthwhile investment for an individual or department involved in the use of synthetic polymers in surgical practice.

A. J. BELLINGHAM

Immunological Aspects of Transplantation Surgery

Edited Roy Calne. 215 × 155 mm. Pp. 342. Illustrated. 1974. Lancaster: Medical and Technical Publishing Co. Ltd. £7·50.

Surgeons who become involved in clinical organ transplantation require a working knowledge of immunology, transplantation biology and genetics in addition to their traditional surgical skills. These subjects are studied mainly by laboratory-orientated scientists who have little opportunity to become conversant with the clinical problems arising in transplantation surgery. The gulf that has always tended to exist between them and their clinical colleagues has become wider in recent years as laboratory techniques have become more complicated and ideas have developed along lines that are sometimes almost incomprehensible to a clinician without special training in the subject concerned.

This book makes a timely attempt to bridge the gulf. It is not a textbook but a collection of essays dealing with the immunological aspects of transplantation biology that attract the most interest, and upon which most research is concentrated at the present time. Professor Calne has assembled a strong team of authors, all of whom are recognized experts in their own fields. There is some repetition but, as Professor Calne explains in the introduction, this has been allowed deliberately so that the reader can see how different contributors interpret the same concepts. Editorial policy has encouraged the authors to distinguish between what is factual and what is speculation. They also try to indicate the phenomena that do not fit in with currently accepted theories because, as Professor Calne points out, it is the study of these that may well lead to new concepts in transplantation biology.

This is a book that will be of great interest to anyone concerned with organ transplantation. Those new to the subject will find it easy to understand. The more experienced will find it a most useful source of up-to-date information.

BERNARD NOLAN

A Synopsis of Anaesthesia

J. Alfred Lee and R. S. Atkinson, Southend. Seventh edition. 184 × 121 mm. Pp. 1000, with 31 illustrations. 1973. Bristol: John Wright & Sons Ltd. £5.

Extending to 1000 pages this edition can hardly be considered a synopsis but rather a complete survey of anaesthesia, containing as it does so much basic medical science as well as clinical anaesthesia and related disciplines such as intensive care.

It will be valuable as a ready guide to most aspects of the subject and by giving many key references as footnotes it facilitates further study. If one were to criticize, there is too little guidance on the relative merits of the multitude of anaesthetic drugs and techniques described; this perhaps is inevitable in a book which attempts to cover so much ground

More succinct are the sections on regional analgesia, a subject to which Dr Lee has contributed so much himself. It is to be hoped that readers of this book will be stimulated to make more use of these frequently neglected techniques.

Undoubtedly the seventh edition will prove to be as popular as its predecessors.

B. A. SELLICK

The Spleen

A. I. S. Macpherson, John Richmond and A. E. Stuart, Edinburgh. 235 × 165 mm. Pp. 280 + ix. Illustrated. 1973. Springfield, Ill.: Charles C. Thomas. $15.75.

This comprehensive monograph on the spleen combines the personal experiences of a surgeon, a physician and a pathologist. They have produced a full and clear account of the organ from all aspects including the anatomical, physiological and pathological. The diagrams, plates and tables are well produced and aid the reader in a general understanding of the subject. Long-accepted facts and theories are given but particular emphasis is laid on areas of controversy or where recent research has produced new concepts. The book covers items of special interest to the surgeon, and at the beginning of each chapter there is a list of its main contents. Both common and rare disorders are discussed, from the pathological, immunological and clinical points of view. We still do not fully understand the position of the spleen in tissue immunology and its relationship with the lymphocytes' transportation of antigen. There is also the question of the role of the small lymphocyte.

Details of and indications for splenectomy and the merits of operation in different types of splenomegaly follow a chapter on investigation by various methods. The pitfalls and complications and possible methods of avoiding these are also included. The likely prognosis following the operation for particular diseases is discussed. This is a book of interest to the specialist surgeon and also to the general surgeon who has occasion to deal with splenectomy for reasons other than trauma. The monograph contains many points which will tend to lower the morbidity and mortality of splenectomy and is an excellent book of reference in the case of splenomegaly of unknown origin.

PHYLLIS GEORGE

Needle Biopsy

Thomas J. Deeley, Cardiff. 220×145 mm. Pp. 170+viii, with 25 illustrations. 1974. London: The Butterworth Group. £3·50.

THIS valuable monograph allows the reader to benefit from the author's great experience with needle biopsy. The first part of the book deals with apparatus, technique, processing of samples and interpretation. A discussion of advantages and limitations of the technique follows, and the risk of dissemination of malignancy is fully treated. It appears that fears that needle biopsy might be harmful are without rational foundation.

The second part of the book describes the application of needle biopsy to lesions in different organs of the body. The author displays an understandable preference for the high speed drill biopsy apparatus that he invented, but where other techniques are preferable or equally suitable they are described too. For each site in which needle biopsy has been undertaken there is useful information on indication, contra-indication, complications and the potential value of results which may be obtained.

The book is particularly well produced with short sections written in lucid English, 25 useful illustrations and about as many tables, an excellent bibliography and a high standard of printing on excellent paper. It will be of especial interest to surgeons and radiotherapists.

J. H. WYLLIE

The Treatment of Chronic Pain

Edited F. Dudley Hart, London. 220×155 mm. Pp. 191+ix. Illustrated. 1974. Lancaster: Medical and Technical Publishing Co. Ltd. £6·50.

THIS is a valuable book on a neglected subject. Dr Hart includes another physician, two surgeons, an anaesthetist and a psychiatrist, and the six authors set out to consider the 'long pain' and how they attempt to control it. Written for general practitioners and senior students, it should surely serve also as a guide to housemen and registrars, who are often perplexed by the number of people with chronic pain whom they find in their constituencies. Teaching on the subject of pain relief has too often been based on the short term experience of the events of acute pain, disregarding the situations of chronic pain. Perhaps no other situation can make a doctor feel more helpless or more tempted to disappear in a cloud of investigations of doubtful value.

Those of us who are unclear how the complex phenomenon of pain is processed will be glad to find a description of the gate theory given as a useful working hypothesis by Huskisson. He considers the measurement of pain and gives a useful summary of trials carried out in various centres with experimental and pathological pain. He provides a comprehensive list of references.

Pain is a process indissolubly bound up with the personality of the sufferer. This is emphasized by each writer and developed in his own way by Szasz, the psychiatrist. He looks at the 'painful person', the person who has adopted the career of being sick and whose pain cannot be influenced by altering the anatomy or chemistry of his body. Such a patient leaves the physician with the dilemma, 'whose pain shall he control?' Provocative as usual, Szasz's contribution adds its own demand to look at the more ordinary person who feels pain in his wholeness.

Hart deals with the rheumatic disorders, which are responsible for more time off work and disability than any other group of diseases. He gives reviews of the different syndromes and the way he dissects his patients in terms of pains to treat. He sums up the indications for the many drugs available but adds 'Every patient, however, is an individual problem child as regards analgesics'. He introduces us to 'typus robustus'; the person who continues at work with active arthritis, has little pain and does not show progressive joint destruction. The importance of activity, distraction and drugs which help less stalwart characters to disregard their pain is emphasized by several of the authors: 'The occupied mind needs less analgesic than the one wide open to all painful stimuli.' Finding that 'Backache' appears as a title in only two of his own row of textbooks of rheumatology he gives a helpful guide to a constructive look at this most common of complaints.

Westbury discusses the treatment of the painful persistent malignant process. He emphasizes that palliative surgery, indicated in some situations, is no substitute for the general understanding of the patient and his problems. He underlines 'the sense of isolation engendered by being passed by which can never be counterbalanced by any amount of skilled pharmacology'. He gives a brief summary of the radiotherapy and chemotherapy which may still be appropriate at this stage and refers to some of the many analgesics available. The reader is given a helpful introduction to this subject, which is perhaps the most common problem of chronic pain a student is likely to meet in the wards of a teaching hospital. He may perhaps mislead some prescribers when he rightly emphasizes that no patient should be kept waiting for a drug until the chosen routine time, and suggests that analgesics should, at this stage, be used readily to prevent pain from occurring at all. The patient will probably do best if his dose is increased, or has the correct adjuvant added, until pain relief covers the routine time and he does not have to ask at all. A busy nurse will find it easier to give him his drugs with her usual round and it is still too often true, as a medical student said recently: 'In our hospital the patients have to earn their morphia.'

White, who considers the non-malignant neuralgias, has followed over 1000 patients, some for many years, and has found a satisfactory outcome in 74 per cent of his patients. He has reviewed the work of many other clinics and refers us to a larger textbook for the details of the surgical procedures that he outlines. His contribution will help to give the general practitioner sufficient knowledge to make informed referrals for such help for their patients. As he points out, however, 'Nature has an extraordinary ability to find new pathways for conducting pain', and he believes that if the effectiveness of stimulating the pain-inhibitor fibres can be improved, the goal of making the surgeon's efforts more consistent with safer methods may come within our reach.

Feldman refers to the use of various chemicals in nerve-blocking procedures. He feels that the patient can best be seen as a complete person in relation to his environment in a pain clinic where various specialties are involved. He describes the methods used where blocking is indicated and considers its place, advantages and drawbacks and in which direction he thinks more refined methods may be developed.

Specialists in the fields covered in these pages will want to turn to the extensive literature referred to; general practitioners, those taking their final exams and many more besides should read this book. It will help them to develop their own practice in the relief of the pain that brings so many of their patients to them. The comment made by a district nurse about some of her patients, 'They don't know how much pain they are supposed to have', should unfortunately be directed sometimes at the doctors who are looking after them.

CICELY SAUNDERS

Central Rhythmic and Regulation: Circulation, Respiration, Extrapyramidal Motor System

Edited W. Umbach and H. P. Koepchen. 265×180 mm. Pp. 418, with 309 illustrations. 1974. Stuttgart: Hippokrates Verlag. No price given.

THIS book contains the proceedings of an international symposium (with 97 contributors) held in Berlin in 1973 under the auspices of the German Neurovegetative Society to discuss rhythmical control phenomena in the central nervous system. Most of the contributions will be of interest only to experienced experimental physiologists, particularly those involved with the respiratory and cardiovascular systems, but a few might usefully attract the attention of neurosurgeons. Unfortunately, however, much of the book is extremely difficult to read (and parts are quite unreadable) because most of the contributions by non-English speakers have been rendered into obscure and inaccurate pseudo-English, including the title of the work itself, which is mistranslated from German and makes no sense in English. As a good deal of the material is of considerable interest to experimentalists, it is a pity that the contributions (some of them from workers of considerable distinction) are not presented in the native language of the speaker. For these reasons, the book cannot be recommended.

BARRY WYKE

Reviews and notices of books

Stroke. Diagnosis and Management. Current Procedures and Equipment

Edited William S. Fields, MD, and John Moossy, MD. 235 × 160 mm. Pp. 298 + xii. Illustrated. 1973. St Louis, Mo.: Warren H. Green Inc. $15.50.

This small book, which is technically an excellent production, contains the deliberations of a symposium on 'Strokes' held under the auspices of the University of Texas Medical School and the Houston Neurological Society.

The contributors and commentators, who include some thirty-four eminent physicians, neurologists, neurosurgeons, neuroradiologists and neuropathologists, were gathered from many well-known centres in the USA.

Most of the presentations are largely of medical neurological interest including sections on blood flow, laboratory diagnosis and coagulation studies and the use and misuse of anticoagulants. There are also chapters devoted to the problems of management of patients with strokes in the community, in family practice and under intensive care in hospital. In addition there are two chapters concerning the use of angiography in diagnosis.

Two chapters only are primarily of surgical interest: one on occlusive disease of the great vessels of the neck and a second providing a general review of the management of intracranial vascular lesions. Neither, well presented though they are, will carry any new message to those specializing in these fields.

Similarly, the chapters on pathology reveal nothing very new to those engaged in the diagnosis and management of cerebrovascular disease. In short, this book, whilst bringing together the views of a number of experts in this field in a very general way, adds nothing to our knowledge of a very common problem.

B. J. HARRIES

Larrey: Surgeon to Napoleon's Imperial Guard

Robert G. Richardson. 222 × 145 mm. Pp. 266 + x. 1974. London: John Murray Publishers Ltd. £4·50.

A good story can be told many times, and the progress of the battles that carried Napoleon all through Europe, Russia and the Near East during those bloody years of the young nineteenth century loses nothing when the account is as seen through the eyes of the Emperor's surgeon and close and trusted friend. Dr Robert G. Richardson writes well, with economy, style and a scrupulous regard for his sources, which include new material from the collection of the Wellcome Institute. All through this excellent book, which is packed with information of compulsive interest, he takes us lightly from one incident to another, all the while filling in a warm and lively picture of the admirable Larrey, from his early revolutionary days on the barricades to the birth of modern warfare in its new *ad hoc* style, free from the formalities of the past, above all with its conservation of the wounded by rapid evacuation and good field surgery in place of disposal by musket-shot—friend and foe alike. Larrey had the indefinable touch of surgical greatness. He was trusted by all, from a wounded monkey to an impatient general, with compassion that was equal for each and successful with both. He could rise to incredible feats such as the personal conduct of 200 amputations in the first 24 hours of the Battle of Borodino. Earlier, in Palestine, we have the lighter moment when Napoleon kept dinner waiting an hour while Larrey finished at the hospital. Napoleon's regard for his surgeon was matched by Larrey's affection for his Emperor. Such was Larrey's depression during the exile in Elba that he was planning to give up everything and join his master when the news reached him of Napoleon's return.

These are a few of the vast number of items from which one could choose in making this review. Their number will only be exceeded by the many more who will read about them for themselves in this most commendable book.

H. H. G. EASTCOTT

Cancer Handbook of Epidemiology and Prognosis

J. A. H. Waterhouse, Birmingham. 250 × 195 mm. Pp. 195 + ix. Illustrated. 1974. Edinburgh: Churchill Livingstone. £6.

Dr Waterhouse has made a considerable contribution to cancer statistics and has an international reputation in the field. This volume is another example of his prodigious industry.

The book provides detailed information on the incidence of and survival from malignant disease in the United Kingdom, the source of the data being the Birmingham Regional Cancer Registry. This registry provides reliable figures on a population of 5 million persons in central England and generally may be taken as representative of the country as a whole. With an efficiency of registration which has exceeded 95 per cent for the past decade, we can be confident of the completeness of the data.

As indicated by Sir Richard Doll in his foreword to the book, accurate continuous cancer registration is of value for a variety of reasons. The accumulating data enable early recognition of changes in the incidence of disease and in results of treatment; changes which may reflect the advent of new cancer risks or the effect of new methods of detection and treatment.

In this volume the material is presented clearly and succinctly in the form of neat labelled line drawings, graphs and tables. The text is correctly kept to a minimum. An occasional exotic touch is added, such as the attractive colour graph illustrating the varying ages of onset of tumours of childhood. The information is classified according to the site of primary disease and provides details of sex and age distribution. The survival data are presented as 5- and 10-year rates, both in crude terms and adjusted by a life table method to allow for mortality from other causes. An interesting inclusion is the separate survival rates for patients given radical treatment.

This is an extremely valuable book, elegantly produced, easy to handle and reasonably priced. It will undoubtedly become a well-thumbed reference book, particularly for those working in the field of clinical oncology.

IAN BURN

The Structure and Biochemistry of Cartilage

A. Serafini-Fracassini, Padua, and J. W. Smith, St Andrews. 240 × 160 mm. Pp. 236 + vii. Illustrated. 1974. Edinburgh: Churchill Livingstone. £8.

Until recently cartilage has been a somewhat neglected tissue in textbooks on the basic medical sciences. Within the past few years, however, several books have been published which give due recognition to the importance of cartilage in its dual roles as the growth medium of the skeleton and the highly specialized lining surface of joints, and to the vast amount of research which is being devoted to this subject at the present time. Few have contributed more to this new knowledge than the two authors of this volume who have successfully bridged the gulf between their respective disciplines of biochemistry and morphology to produce one of the most up-to-date and comprehensive accounts of cartilage biochemistry and structure.

The book is well illustrated with electron micrographs of excellent quality, although the legends are sometimes inadequate for one not entirely familiar with this medium. The clinician may regret that there is no attempt to relate this wealth of information on normal cartilage to the changes occurring in the disordered state, but this is not the authors' purpose. They have set out to 'bring together some of the existing biochemical, morphological and physiology knowledge of cartilage', and this modest objective has certainly been achieved. This book will be essential reading for all researchers on the connective tissues. Rheumatologists and orthopaedic surgeons will find it a useful work of reference, for the informative text is enriched by an extensive bibliography—nearly 400 items for a single chapter! Not a book for the bedside table, but one which should be available in all medical libraries.

JOHN CHALMERS

ACM endoscopes leave nothing to the imagination

Most surgeons today recognise the superiority of endoscopy as a means of confirming diagnoses of colon diseases. It can be quicker and easier than laparotomy, and is also less traumatic for patients and makes fewer demands on hospital facilities.

The premier instrument for colonic investigations is the ACM F9L coloscope. Advanced features include 12X magnification and a sharp, wide angle circular image three times larger than competitive instrument's.

With it a surgeon can clearly view as far as the caecum, take biopsy specimens and perform polypectomies. After surprisingly little practice, coloscopy can be most rewarding. And the ACM coloscope is exceptionally easy to use – a single, one-handed joystick controls the poly-directional tip.

There's a shorter version, too, the F9S which will reach to the transverse colon and beyond. For the experienced coloscopist there's the dual channel F9A, a major operative, as well as diagnostic instrument.

To find out more, please use the coupon. Or write or telephone.

Please tell me more about ACM endoscopes.
I would like literature only ☐
Please arrange a visit
My telephone number is ☐
Name
Address

B.J.S 2·75

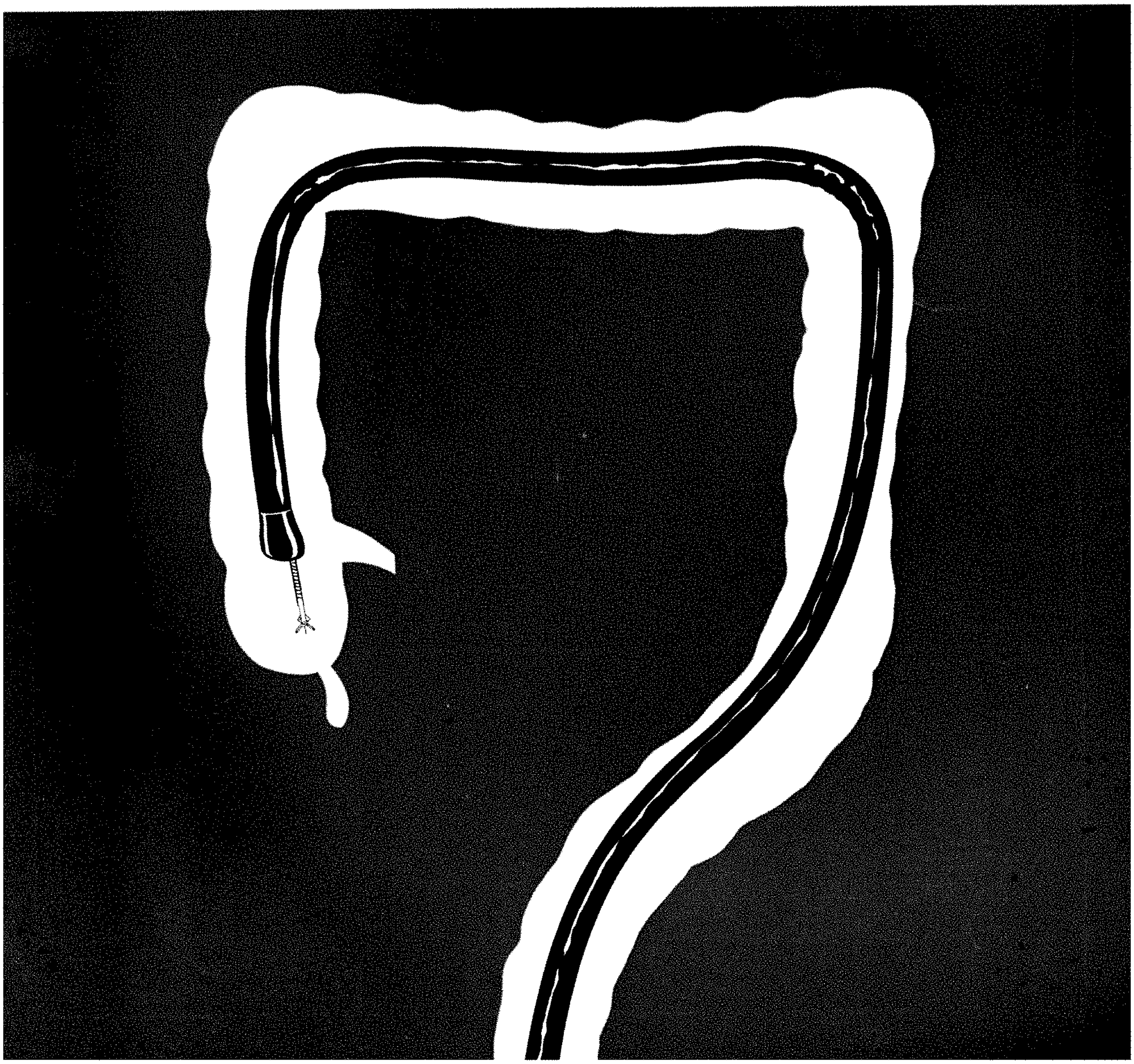
ACM Endoscopes – clearly the best

ACM

Wappler Endoscopy Limited,
Park House, 22 Park Street, Croydon, Surrey, CRO OYH
Telephone: 01-686 4241

WAPPLER Endoscopy Limited

ACM endoscopes for gastro-enterology, bronchoscopy, urology, gynaecology and teaching.



YELLOW ALERT!

When deep vein thrombosis is extending put them on Kabikinase to dissolve the clot, preserve the valves and restore the flow. (Lysis achieved, anticoagulate with heparin to prevent rethrombosis.)

KABIKINASE

(pure streptokinase)

Full information, brochure and wall card on request.

Kabikinase is manufactured by AB Kabi, Stockholm, Sweden, and is available only from:

KabiVitrum Ltd
Bilton House, Uxbridge Road,
Ealing, London W5 2TH.
Telephone: 01-567 4717 01-579 1871

P.L. No. 0022/5006
Kabikinase is a registered trade mark.

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU

"I Bring Peace"-73

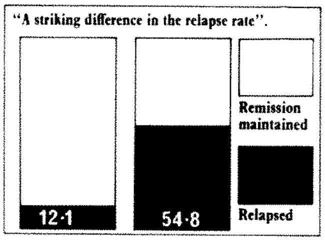
"It is concluded that maintenance treatment of ulcerative colitis with sulphasalazine (salazopyrin) should be continued indefinitely unless contraindicated by side effects".[1]

The results of the above controlled trial carried out at the Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford are all the more welcome as earlier trials of cortisone[2] and prednisone[3] at standard dosages have shown them to be ineffective in reducing the number of recurrences of ulcerative colitis.

"Fortunately, Sulphasalazine tablets, 0.5 grams 4 times a day will prevent relapses in the majority of patients with colitis, and only a few patients cannot tolerate this relatively small dose, which can be continued indefinitely since we do not know when, if ever, it can be safely stopped".[4]

Salazopyrin (sulphasalazine) is available as the plain 0.5g. tablet, 0.5g. EN-tab and as an 0.5g. suppository. Literature and detailed information on Salazopyrin are available on request.

Salazopyrin is a registered trade mark.



"The patients who received dummy tablets had more than four times the relapse rate of those receiving sulphasalazine".[1] (Salazopyrin®).

Both groups of patients had been satisfactorily maintained for 1–5 years on Salazopyrin prior to the study, in which they took Salazopyrin or placebo for 6 months.

References
1. Gut (1973) *14* 923–926
2. Brit. med. J. (1959) *i* 387–394
3. Lancet (1965) *i* 188–189
4. General Practitioner (1972) April 7 p11

Salazopyrin

– to be continued indefinitely

Further information on request from:–
Pharmacia (Great Britain) Ltd.
Paramount House,
75 Uxbridge Road,
London W5 5SS.
Telephone: 01-579 0102/7

Pharmacia

Vol. 62 : No. 3 : March 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

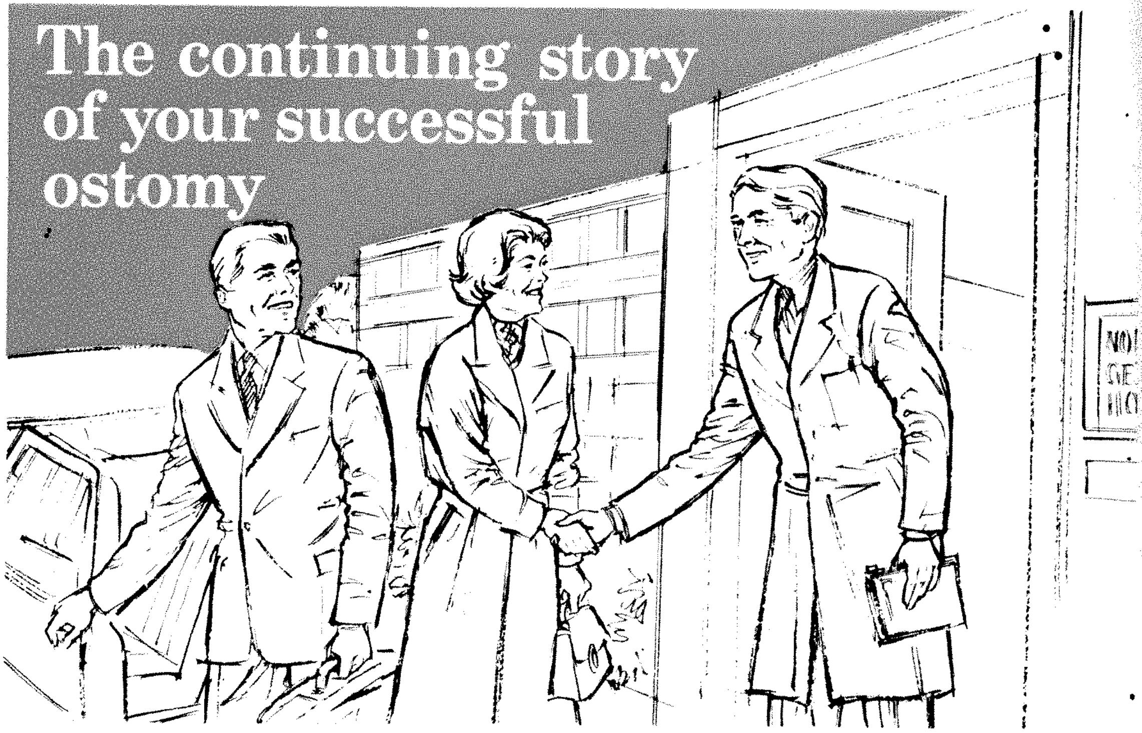
*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society)
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN MCADAM Kampala : Uganda
A. C. MCEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX
Subscription £15 per annum, post free. Single copies £1·50, post free

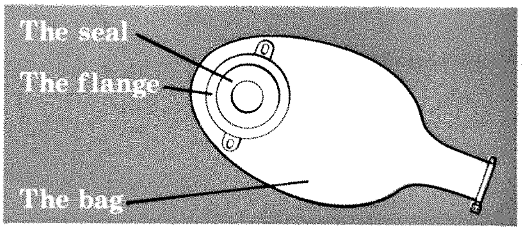
THE WILLIAMS & WILKINS CO., BALTIMORE
Second Class Postage paid at Baltimore, and at additional mailing offices.



The continuing story of your successful ostomy

Good reasons why REDIFIT is the ostomy appliance for your patient.

Redifit will give added comfort and confidence to the Ostomist because it incorporates the following distinct advantages:



THE SEAL

The seal is of a superior Karaya gum which will not cause any irritation to the most sensitive skin. It will not distort, and will always create a perfect seal with the skin. It is less affected by extremes of temperature and humidity and so will always come to you in perfect condition.

THE FLANGE

This is a new pattern, unique to Redifit. It is not fastened directly to the bag but is held by a collar on which it can rotate. Therefore even after the bag is fixed in position, the angle of the flange can be adjusted to give the most comfortable position for the belt.

THE BAG

Redifit bag has no less than five laminations of plastic, and is guaranteed odour-proof for the normal life of the bag.

With only one layer of film, one cannot be sure of avoiding the embarrassment of escaping odour.

COMPETITIVE COST

Redifit for the special needs of special people

Downs Surgical Ltd

CHURCH PATH, MITCHAM, SURREY 01-648 6291

The British Journal of Surgery

Vol. 62 : No. 3 : March 1975

Original papers

		Page
Haemorrhagic and necrotizing pancreatitis	Geoffrey Glazer	169
Plasma catecholamines in severely injured patients: a prospective study on 45 patients with multiple injuries	A. Jäättelä, A. Alho, V. Avikainen, E. Karaharju, J. Kataja, M. Lahdensuu, P. Lepistö, P. Rokkanen and T. Tervo	177
The early detection of postoperative deep vein thrombosis: an assessment of Doppler ultrasound, physical examination and the temperature chart	C. R. K. Rickford and David Negus	182
Surgical management and problems of heart pacing	J. Borrie and I. Lichter	186
Postoperative problems and management after hepatic resection for blunt injury to the liver	T. Vajrabukka, A. L. Bloom, M. Sussman, C. B. Wood and L. H. Blumgart	189
The application of the $^{99}\mathrm{Tc}^{m}$ phosphate bone scan to the study of breast cancer	D. L. Citrin, R. G. Bessent, W. R. Greig, N. J. McKellar, C. Furnival and L. H. Blumgart	201
Cystic thyroid nodules	Michael K. G. Ma and G. B. Ong	205
Thyroid cancer: twenty years' experience in a general hospital	D. J. Campbell and R. H. Sage	207
Motility changes in the antrum after proximal gastric vagotomy	Malcolm Kelly and Terence Kennedy	215
The management of bleeding acute gastric erosions: the role of gastric hypothermia	H. S. Himal, W. W. Watson, C. W. Jones and L. D. MacLean	221
A case of haemorrhage from volvulus of the gastric fundus	C. Metcalfe-Gibson	224
Is 'second look surgery' justified in suspected recurrences of cancer of the stomach?	Harold Ellis and G. Jayasekara	226
Flatulent dyspepsia in patients with gallstones undergoing cholecystectomy	R. D. Kingston and C. W. O. Windsor	231
Traumatic haemobilia	E. Vallidis and N. Papalexandris	234
Gumma of the liver	Roger Parnis	236
Rupture of subcapsular haematoma of the liver in a case of eclampsia	C. H. Browne, Gillian C. Hanson, L. R. De Jode and P. A. Roberts	237
Single layer anastomosis after rectosigmoid resection	N. A. Matheson and A. D. Irving	239
Temporary transcaecal ileal diversion in prevention of anastomotic leak in planned colonic surgery (an alternative to proximal colostomy)	Alan Simpson and V. K. Srivastava	243
A colostomy/ileostomy construction clamp	Laurence Tinckler	246
Ureteric obstruction due to sigmoid diverticulitis	B. I. Rees and P. M. Bolton	247

Reviews and notices of books

250

© John Wright & Sons Ltd and the respective contributors named above, 1975.
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.

Why run the risk of her cystitis ascending, and the problem of pyelonephritis developing? Rapid, effective therapy with SEPTRIN is indicated at the first opportunity.

SEPTRIN was rated top oral treatment in a British survey of 23,491 urinary pathogen sensitivities.[1] SEPTRIN has been judged superior to ampicillin[2,3] and is now well established as a first-line treatment for urinary infections.

SEPTRIN contains trimethoprim and sulphamethoxazole
Full prescribing information is available on request.

1 *Postgrad med J.* (1971) **47**, Supplement (September), 7.
2 *Brit med J.* (1972) **2**, 673.
3 *Clin Trials J.* (1972) **9/3**, 9

Wellcome

Wellcome Medical Division,
The Wellcome Foundation Ltd.,
Berkhamsted, Herts

SEPTRIN

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 60. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISEMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are two or more authors (apart from the main author), these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title

of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature* (*Lond.*) **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea **4**, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th ed. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology.* London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BEAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

Congress Proceedings

CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding. or that following.,

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)

INJURY

The British Journal of Accident Surgery

Editor, R. L. BATTEN, FRCS(Eng)

Injury provides a focal point of information for those engaged in the many fields of medicine which accident surgery involves. Contributions from all over the world provide well-organized and comprehensive coverage of every aspect of care of the injured. Original articles take up a large section of INJURY and, as accident surgery is so often concerned with the individual patient, reports of interesting and complex cases are included. To keep the reader informed of the latest progress, INJURY contains details of current research and of new drugs and medical instruments. Reviews of new books appear regularly and, of particular value in a field of medicine which often has a debt to other specializations, INJURY devotes some of its space to abstracts from a wide range of publications on related subjects.

Published Quarterly

Annual Subscription: £8·50 (post free)

Single Numbers: £2·40 (post free)

BURNS including Thermal Injury

The Journal of the International Society for Burn Injuries

Editor, J. E. LAING, FRCS

To counter the high mortality and morbidity caused by burn injuries needs the teamwork of a wide range of specialists: treatment of the patient can involve plastic, paediatric and orthopaedic surgeons, biologists, immunologists and bacteriologists, while the rehabilitation of the patient can need the efforts of occupational therapists, physiotherapists, psychiatrists and social workers. This new journal is published to foster the exchange of information amongst all those engaged in preventing and minimizing the effects of burn injuries. BURNS is sponsored by the International Society for Burn Injuries, whose aims are to transcend national boundaries in improving the prevention and care of burns by education, research, practical advice and assistance, and the encouragement of cooperation between all countries and all specialists.

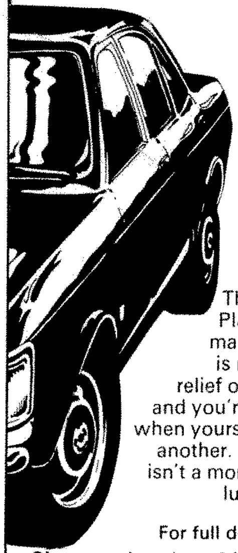
Published Quarterly

Annual Subscription: £8·50 (post free)

Single Numbers: £2·40 (post free)

JOHN WRIGHT

42–44 Triangle West, Bristol BS8 1EX



NEW CAR?

NO CAPITAL OUTLAY

The Clearway Executive Leasing Plan offers you the choice of any make or model, what's more there is no capital outlay and 100% tax relief on your annual leasing charges, and you're never without a car, because when yours is being serviced we lend you another. For the professional man there isn't a more economical way of ensuring luxurious, trouble free motoring.

For full details contact:
Clearway Leasing, 11 Belmont, Lansdown Road,
Bath BA1 5DZ (Tel: 60463)
An Oliver Rix Company

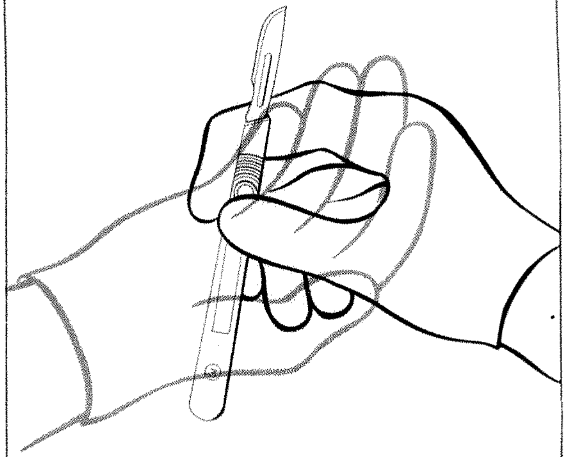
BRITISH JOURNAL OF SURGERY

Binding Cases

Binding cases for Volume 61 may be obtained from the Publishers at £2·00 post free. They are supplied in dark red cloth with imitation gold lettering on the spine.

If desired, the publishers will undertake the binding at an inclusive charge of £7·50, post free.

JOHN WRIGHT
42–44 TRIANGLE WEST
BRISTOL BS8 1EX



Another surgeon is about to use one of the world's finest surgical blades.... ...this happens thousands of times every day!

It happens because the blades are by Swann-Morton, the people who meet the highest requirements in surgical knives.

We need say very little about our superiority. The world's surgeons have proved it for us!

Swann-Morton

SWANN-MORTON LIMITED
PENN WORKS, OWLERTON GREEN
SHEFFIELD S6 2BJ. ENGLAND.

SIEMENS

DIATHERMY EQUIPMENT
for modern
ELECTRO-SURGICAL
TECHNIQUES

Available in various designs such as

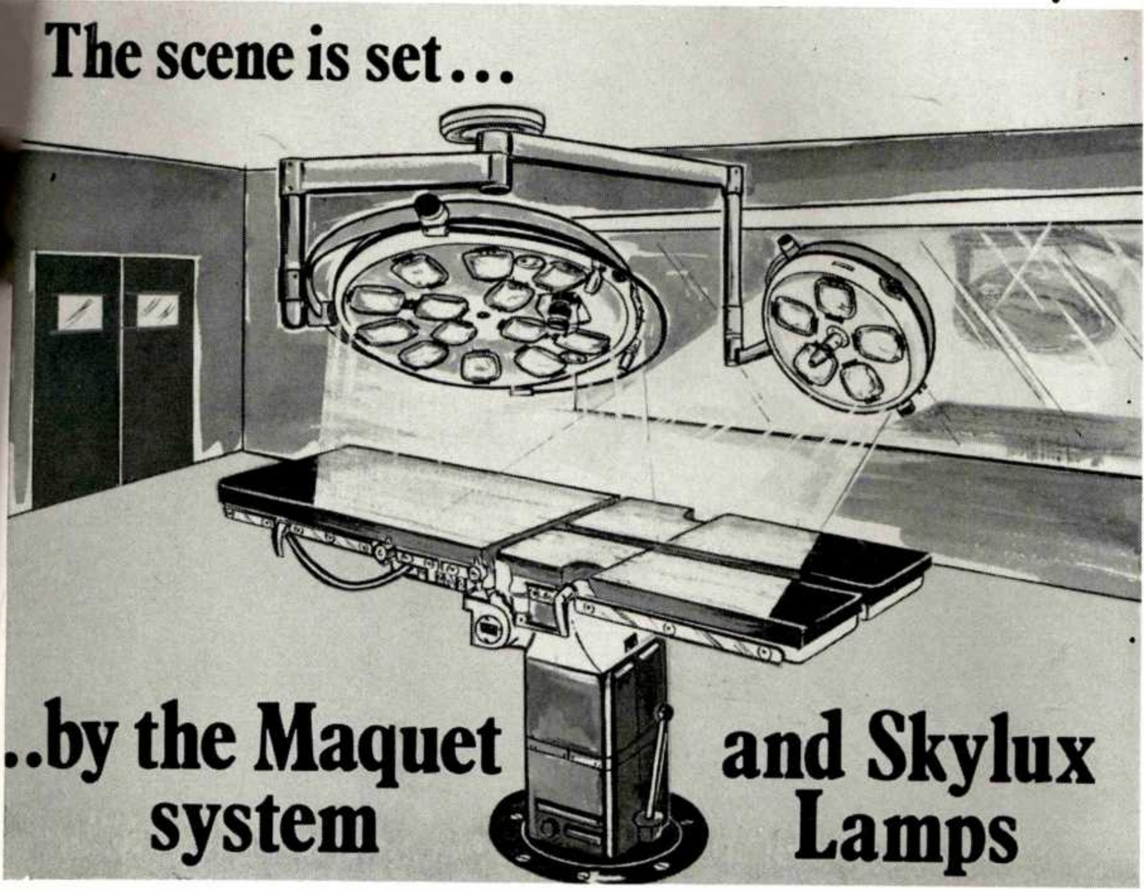
TROLLEY MOUNTED,
CEILING SUSPENSION
or installation in the
OPERATING THEATRE WALL

Full details available on request

Sierex

SIEREX LIMITED Electro-Medical Department,
Heron House, 109 Wembley Hill Road,
Wembley HA9 8BZ. Telephone 01 903 0418

Branches in Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester, Newcastle and Reading. Agents in Belfast.



Maquet fixed column operating table system

Fixed column–power operated
Extreme stability
Free access for x-ray equipment
Wide variety of table tops
Tops easily interchangeable–increased theatre efficiency
Unique 'Tele' control
Easy clean finish

Skylux Lamps – for all Theatre applications

- High level of light intensity
- Maximum freedom from shadow and glare
- Ideal variation of illumination
- Heat free
- A real white light
- Easy mobility

Catalogues available on request

Downs Surgical Ltd

CHURCH PATH, MITCHAM, SURREY 01-648 6291

GU

NEW

DIATHERMY
FORCEPS,
SCISSORS &
SCALPEL HANDLES
COVERED
WITH
LONG-LIFE..

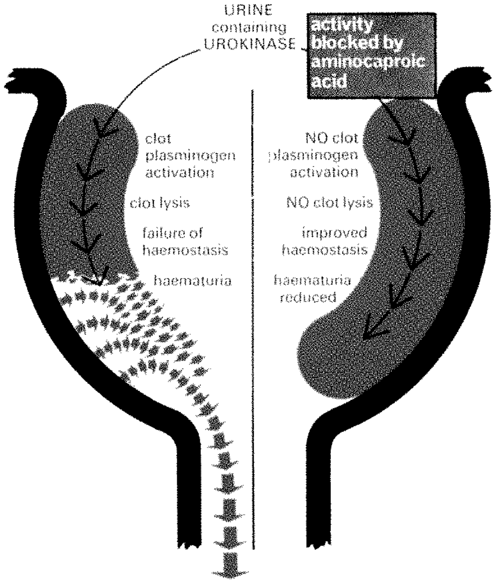
Insulast

- Developed for autoclaving
- ECONOMICAL · saves on repairs
- SAFER · crack resistant
- THINNER · better grip
- Universal cable fitting

When ordering new diathermy instruments, or requiring old instruments to be re-insulated, always specify 'INSULAST' only obtainable from;

The G.U. Manufacturing Co. Ltd.
28a, Devonshire Street, London, W1N 2AJ
Telephone; 01-935-2835.

The mechanism of post-prostatectomy bleeding and EPSIKAPRON® control



Epsikapron (aminocaproic acid) is rapidly excreted in the urine in high concentration; there it inhibits urokinase, the fibrinolytic enzyme in urine. With the haemorrhage-sustaining property of urine blocked, the haemostatic coagulum becomes adequate, and blood loss is diminished substantially.

Epsikapron makes your prostatectomy patient's post-operative course smoother by diminishing:

the need for post-operative blood transfusion
clot retention
catheterization
the risk of infection
the period of hospitalization

Presentation

Epsikapron Solution for Injection 0.4 g/ml Box of 6 ampoules of 10 ml, each containing 4.0g aminocaproic acid (0022/5003) Epsikapron Effervescent Powder 50% Box of 30 sachets, each containing 3.0g aminocaproic acid (0022/5004) Epsikapron Syrup 0.3g/ml Bottle of 250ml (0022/5005)

EPSIKAPRON®

Manufacturer: AB Kabi, Stockholm, Sweden.
Further information from:
KabiVitrum Ltd
Bilton House, Uxbridge Road, Ealing, London W5 2TH.
Telephone: 01-567 4717 or 01-579 1871.

The British Journal of Surgery

Vol. 62 : No. 3 : March 1975

Br. J. Surg. Vol. 62 (1975) 169–176

Haemorrhagic and necrotizing pancreatitis

GEOFFREY GLAZER*

ACUTE pancreatitis may be a relatively innocuous oedematous reaction or less frequently a severe haemorrhagic and necrotic destruction of the gland. Current views suggest that the latter is an extension of the oedematous reaction rather than a separate entity.

Mortality

A review of published series throughout the world reveals a wide range of mortality which is probably the result of geographical differences (and hence differences of associated aetiological factors), problems in diagnostic classification and variations in treatment. Different series may not be strictly comparable or may be weighted by high or low risk cases: on the one hand, elderly patients or those with postoperative pancreatitis, and on the other hand, patients having their second or third attack. Nevertheless, some broad conclusions can be drawn. The overall mortality of pancreatitis throughout the world varies between 10 and 23 per cent (Zimberg, 1968), with similarly high figures in the United Kingdom (Pollock, 1959; Trapnell, 1972). Haemorrhagic pancreatitis occurs in 10–25 per cent of all cases; the mortality in these patients is much higher, with death rates between 40 and 70 per cent (Barraclough and Coupland, 1972).

Intraduodenal digestion

The exocrine pancreas secretes a large volume of juice which contains water, electrolytes and several digestive enzymes. The proteolytic enzymes exist in this juice as inactive pro-enzymes which become activated in the duodenum by the hormone enterokinase. The key reaction is the conversion of trypsinogen to trypsin, as this then activates the other proteolytic pro-enzymes. Some other enzymes (i.e. prophospholipase A) are activated in the duodenum by bile and calcium ions, while yet others are secreted in their active form (i.e. amylase). Thus, there begins within the duodenum a considerable digestive ferment which is delicately controlled by a complex neurohumoral mechanism. Hermon-Taylor (1972) has recently reviewed this topic more fully for surgical readers.

Development of pancreatitis

There are two stages in the development of acute pancreatitis that must be differentiated; first, the initiation of the condition during which the pancreatic defence mechanisms are overcome and acinar cell damage results, and secondly the pathogenesis of pancreatic necrosis once the initial insult to the gland has occurred. An understanding of the various steps in the progression from oedematous pancreatitis to pancreatic necrosis would lead to a more rational therapeutic approach, but in our present state of knowledge many of these steps are hypothetical.

Pancreatic defence mechanisms

The pancreas possesses several defence mechanisms which prevent autodigestion but once these are overcome pancreatic 'damage' at acinar cell level occurs and pancreatitis ensues. The enzyme-secreting acinar cell protects itself from destruction by storing its enzymes in capsules away from the main cellular components, and by activation of the pro-enzymes in the duodenum. The pancreas also produces a specific pancreatic trypsin inhibitor (PTI), but the importance of this polypeptide in preventing the intrapancreatic activation of trypsinogen is not clear. A fall in the level of PTI secreted on the first postoperative day has been demonstrated in a small group of patients (Morgan et al., 1968), and this finding may be of aetiological significance in postoperative pancreatitis. The pancreatic ductal cells may provide another defence mechanism, but this can be breached under certain circumstances. Perfusion of bile through the duct under physiological pressures will cause no injury, but injection at higher pressures will cause a rupture of the finer ducts. Bile infected with *Escherichia coli* causes a mucolytic and cytotoxic effect on the ductal cells in the cat (Konok and Thompson, 1969), but the relevance of this to the human situation is not known. Retrograde injections into the duct are now performed in man via a fibreduodenoscope in order to obtain pancreatograms. This procedure was associated with abdominal discomfort in a few patients, but almost 50 per cent of these patients had a rise in serum amylase of up to three times the normal value (Cotton et al., 1972). The integrity of the pancreatic duct sphincter is of importance in the prevention of reflux, as is the positive pressure gradient from pancreatic duct to duodenum.

---

* Surgical Unit, St Mary's Hospital, London W2.

Associated clinical conditions

Biliary tract disease, alcoholism and a miscellaneous group which comprises such diverse conditions as hyperparathyroidism, trauma, infections, postoperative cases, hereditary defects, hyperlipidaemia, drugs and pregnancy are all associated with pancreatitis. In a substantial number of cases of acute pancreatitis there is no obvious associated clinical condition, and this idiopathic group accounts for 40 per cent of the cases reported by Trapnell (1966).

Initiating mechanisms: The manner in which the above conditions initiate pancreatitis is varied and it is proposed to discuss only the main groups of biliary tract disease and alcoholism. For information on the miscellaneous group the reader is referred to recent reviews (Creutzfeldt and Schmidt, 1970; Banks, 1971; Geokas, 1972).

Biliary tract disease: The explanation of the association between biliary tract disease and pancreatitis has been largely based on the reflux theory of altered bile into the pancreatic duct. Little is known of the factors that control or prevent such reflux in man but more is known of the various 'toxic' components in bile that can cause pancreatitis. Unconjugated bile salts (produced by bacteroides, *Streptococcus faecalis* and clostridia) and lysolecithin (produced by the pancreatic enzyme phospholipase A acting on bile lecithin) have both been shown to be damaging to the pancreas (Schmidt and Creutzfeldt, 1969). A mixture of *E. coli* and bile damages pancreatic ductal cells (Konok and Thompson, 1969), and this may be due to the bacteria converting bilirubin diglucuronide to free bilirubin or to some other unidentified compound (Banks, 1971).

Another theory on the relationship between acute cholecystitis and pancreatitis suggests that there is a retrograde spread of 'infection' by lymphatics, as this connection between the two organs has been demonstrated experimentally in the dog (Weiner et al., 1970).

Alcoholism: Kalant (1969) in his review of this topic has pointed out that there are several theories with little sound evidence to explain the known association between alcoholism and acute pancreatitis. One suggestion is that pancreatitis is caused by stimulation of pancreatic secretion coupled with spasm of the sphincter of Oddi (Schapiro et al., 1966). Secretion is stimulated first by the release of gastric acid which then promotes the release of secretin, and secondly by gastrin which acts directly on the pancreas in promoting secretion (Walton et al., 1962). There is some evidence that spasm of the sphincter of Oddi is produced by alcohol (Pirola and Davis, 1968). However, hypersecretion and ductal obstruction have been shown experimentally to produce only pancreatic oedema and not pancreatitis.

Another theory proposes an alteration in bile constituents by alcohol. Injection of bile into the pancreatic duct of the rat produces haemorrhagic pancreatitis. This reaction is more severe if the bile is obtained from animals intoxicated with alcohol (Gamklou and Edlund, 1966), but the nature of this 'alcoholic' bile is unclear.

The possibility of a cellular or a metabolic derangement of the acinar cells leading to pancreatitis has also been raised by several workers. Acinar cell changes of cytoplasmic degradation, mitochondrial swelling and lipid accumulation in rats on a chronic ethanol regimen have been demonstrated (Darle et al., 1970), whilst other work has shown an inhibition of ^{32}P uptake into pancreatic phospholipids in rats following long term ethanol ingestion, suggesting a metabolic defect (Orrego-Matte et al., 1969). Precisely how these changes may induce acute pancreatitis or make the gland more vulnerable is still not known.

It is of interest that Gillespie (1973) has recently found the incidence of alcoholism or a precipitating bout of drinking to be 23 per cent in a review of 93 cases of pancreatitis from the Edinburgh area. This figure is much higher than that quoted in other series from the United Kingdom and the author attributes this to either a concealment by the patient of his drinking habits or a higher rate of alcoholism in the Edinburgh area compared with the south of England.

Reflux of activated duodenal enzymes

McCutcheon (1968) has argued persuasively against the two older theories of the causation of pancreatitis, namely the theory of hypersecretion and ductal obstruction and the common channel theory of bile reflux. He has proposed instead the reflux of activated duodenal enzymes as the unifying concept in the initiation of acute pancreatitis.

The experimental evidence for duodenal reflux is based largely on the Pfeffer loop (Pfeffer et al., 1957). In this canine model a haemorrhagic pancreatitis can be induced regularly by the creation of a closed duodenal loop. If the pancreatic ducts are ligated the pancreas is protected, which suggests that reflux is the mechanism of action. This model has been compared with the human situation following partial gastrectomy. There was a much higher incidence of deaths from postoperative pancreatitis after a Polya gastrectomy (12 deaths in 1769 cases) compared with Billroth 1 gastrectomy (no deaths in 605 cases) in the series reported by Wallensten (1958). This is attributed by McCutcheon (1968) to the potential closed afferent loop in the Polya gastrectomy, and he quotes other clinical situations such as annular pancreas and duodenal diverticulum where a potential closed loop may be the cause of reflux and pancreatitis. The Pfeffer loop model can be modified in ways which suggest that the ensuing pancreatitis is caused by different mechanisms. If the bacterial flora within the loop is inhibited by topical antibiotics the incidence of haemorrhagic pancreatitis is reduced (Kune, 1968b; Williams and Byrne, 1968). Against this bacterial theory is the evidence that pancreatitis develops in germ-free dogs who have a Pfeffer loop (Nance and Cain, 1968), but it is possible that vascular compromise of the loop is of importance. In their original description of the experiment, Pfeffer et al. (1957) concluded that mucosal ischaemia in the loop was vital for the production of pancreatitis. This view has been further substantiated by experimental work in which the loop was decompressed; this prevented both mucosal ischaemia and the development of pancreatitis (Rosato et al., 1970). The conclusion from these experiments is that bacterial, ischaemic and enzymatic factors are contributing to the pancreatitis and that 'toxic' elements caused by the interaction of blood, bacteria and enzymes may be involved in different situations.

If McCutcheon's (1968) theory is correct then the function of the lower end of the pancreatic duct must be a critical factor in preventing pancreatitis. Damage or distortion of this sphincter is suggested in several situations. A gallstone impacted at the ampulla may produce a fixed dilatation of the duct, whilst the long arm of a T-tube may act as a splint and prevent closure of the duct. Alcoholic pancreatitis is explained by local damage to the papilla with oedema and incompetence. The possibility of vomiting induced by alcohol with a rise in duodenal pressure and pancreatic reflux is also suggested. With regard to the association between gallstones and pancreatitis, McCutcheon (1968) proposed the novel idea that both conditions arise as a result of duodenal reflux, and pancreatitis is only secondary to gallstones in the occasional case when a stone is impacted at the ampulla. He stated correctly in favour of his thesis that cholecystectomy and eradication of the biliary tract disease do not necessarily protect against further attacks of pancreatitis, but nevertheless his bald statement that 'there is no mechanism by which stones in the gall bladder can cause pancreatitis' may only be a reflection of our poor state of knowledge rather than a proved fact. The lymphatic connections between the two organs may be one such mechanism (Weiner et al., 1970).

Using another argument McCutcheon (1968) reasoned that sphincterotomy did not decrease the incidence of pancreatitis because reflux was continuing. It has, however, been shown that the much more effective operation of sphincteroplasty does reduce further attacks of pancreatitis (Jones et al., 1969) and so this argument is open to question.

At the moment the initiating role of the duodenal reflux must be considered a possibility in some cases of pancreatitis.

Pathogenesis

Once damage has occurred to the acinar cell there follows a series of changes within the gland which are poorly understood. Thus the role of the various pancreatic enzymes remains a matter of conjecture. Proteolytic enzymes have been recovered in an active form from pancreatic tissue in experimental acute pancreatitis, and trypsin and chymotrypsin can cause pancreatic inflammation when injected into the pancreatic duct. It is probable that the main action of trypsin is to activate the enzymes elastase and phospholipase A (Creutzfeldt and Schmidt, 1970) and possibly kallikrein. Elastase, which causes the dissolution of elastic fibres in blood vessels, appears important in the transition of oedematous to haemorrhagic pancreatitis, and a high level of elastase has been found in the pancreas of patients dying with haemorrhagic pancreatitis (Geokas et al., 1968). Phospholipase A is important in the development of pancreatic necrosis by its production of lysolecithin from bile lecithin. Higher levels of lysolecithin and lowered levels of lecithin have been found in glands that have undergone necrosis (Schmidt and Creutzfeldt, 1969). Ischaemia of the pancreas is a major factor in the development of haemorrhagic pancreatitis and necrosis. This may be due to several factors (Goodhead, 1969a): venous stasis (Anderson, 1963), release of vasotoxic substances (Anderson, 1961), the activation of pro-elastase (Geokas et al., 1968), the release of intracellular enzymes (Reid et al., 1958; Weissmann, 1965) and periacinar lymphatic occlusion (Anderson and Schiller, 1968). All may contribute to the vicious circle of vascular occlusion, thrombosis, increasing tissue anoxia and necrosis. A clear understanding of the processes leading to necrosis would give a basis for a rational prophylactic therapeutic regimen to be instituted.

The role of kallikrein in causing systemic hypotension has undergone critical study (Ofstad, 1970). It is known that pancreatic exudate contains strong kininogenase activity and that the plasma kinins released by kallikrein cause increased vascular permeability. Pancreatic exudate releases histamine from mast cells (Ofstad et al., 1969), and as this cannot be done by kallikrein some other factor may be present which contributes to the hypotension. Prostaglandin-like activity rises in the pancreatic venous effluent in experimental pancreatitis and high levels are found in the peritoneal exudate (Glazer and Bennett, 1974). The role of these substances in the hypotensive and pain responses remains to be elucidated.

Diagnosis

There is no completely reliable method of diagnosing acute pancreatitis apart from laparotomy. A classic clinical picture and a serum amylase above 1000 Somogyi units will usually give the diagnosis, but this picture is often confusing and may mimic several other abdominal crises such as acute cholecystitis, perforated or penetrating ulcer, bowel infarction and leaking or dissecting aneurysm. The laboratory aids to diagnosis are non-specific. A high serum amylase is often found in other conditions, and the level will also depend in part upon the timing of the blood sample. It is also a poor reflector of the severity of pancreatitis. The renal clearance of amylase increases in pancreatitis and the ratio of this clearance to creatinine clearance may be of diagnostic value (Levitt et al., 1969). Serum lipase levels were not considered helpful by Trapnell (1966) but may be of some value when improved methods of measurement are employed (Song et al., 1970). The level of serum catalase is elevated in pancreatitis and falls more slowly than serum amylase. Although this enzyme is not specific it has been recommended (Meszaros et al., 1973); these authors also described a new sensitive method of estimating catalase levels.

There are no specific clinical features of haemorrhagic as opposed to oedematous pancreatitis (Winstone, 1965); the presence of Grey-Turner's or Cullen's sign is a rare and late manifestation of the disease. Bruising in the flanks soon after the onset of acute abdominal pain should raise the possibility of a leaking abdominal aneurysm rather than pancreatitis.

The presence of methaemalbumin in the serum is not diagnostic of haemorrhagic pancreatitis and may occur in other acute conditions such as bowel strangulation, gastro-intestinal haemorrhage and soft tissue trauma (Battersby and Green, 1971). Furthermore, elevated levels are not always found in haemorrhagic pancreatitis. However, when the diagnosis has been established the plasma level of methaemalbumin is one of several parameters which are of importance in assessing and prognosticating about the course of the illness (Trapnell, 1966).

Clinical aspects

Clinical effects are systemic and local. The most important systemic effect is shock, which is the consequence of the loss of fluid into the retroperitoneal tissues and peritoneal exudate. Shock is probably increased by the release of vasoactive substances. Other systemic effects may include ileus, cardiorespiratory failure, renal failure, psychosis, coagulopathies and the metabolic changes of hypocalcaemia, hypomagnesaemia, hyperlipidaemia and hyperglycaemia.

The phase of cardiorespiratory failure may occur in the first 2 or 3 days; this syndrome appears to be less common in the United Kingdom than in other countries, a fact attributed to differences in the aetiological background of the disease. Hypoxaemia (Po_2 below 75 mm Hg) was found in 58 per cent of 40 unselected patients with early pancreatitis (Ranson et al., 1973). These workers and others (Kellum et al., 1972) stressed the insidious nature and seriousness of this complication. The diagnosis at an early stage can only be made by blood gas analysis. The autopsy findings in the lungs are of congestion and diffuse areas of microscopic atelectasis (Gliedman et al., 1970). The cause of these changes is not known although circulating lecithinase has been incriminated; elevated levels of serum lecithinase have been found in patients with pancreatitis (Zieve and Vogel, 1960) and this is known to cause pulmonary surfactant changes when infused into dogs (Morgan et al., 1965). The presence of pleural effusions, a high diaphragm and increased metabolic demands will also contribute to the respiratory embarrassment. It is probable that the pulmonary changes in pancreatitis are non-specific and are similar to those found in a variety of other shock states and injuries (Blaisdell and Schlobohm, 1973). From a clinical point of view an increased awareness of the respiratory problem should lead to routine arterial blood gas analysis. A patient who develops a psychotic state is likely to be hypoxaemic, and delirium tremens should only be considered when blood gases are found to be normal.

Renal failure, defined as a rise in blood urea to above 100 mg/100 ml or when there were post-mortem changes of acute tubular necrosis, was found in 15 per cent of 41 patients treated by Gordon and Calne (1972). They suggested that the cause of the failure may be more complex than simple hypotension and fluid loss and postulated that toxic products of pancreatic autodigestion are contributing to the response.

There have been recent suggestions that the hypocalcaemic response in acute pancreatitis may be due to more than the deposition of calcium in fat necrosis. One theory is that glucagon, released in acute pancreatitis (Banks and Janowitz, 1969), may stimulate the release of thyrocalcitonin which would cause inhibition of bone resorption and hypocalcaemia (Avioli et al., 1969). Another theory suggested that the hypocalcaemia is secondary to hypomagnesaemia (Muldowney et al., 1970) which makes the bone refractory to the action of parathormone. The cause and precise incidence of hypomagnesaemia in pancreatitis are not known. More information is required before the cause of the hypocalcaemia can be determined but it seems clear that a low level of serum calcium (below 7·5 mg/100 ml) is associated with a bad prognosis (Trapnell, 1966).

The local effects of the disease in the abdomen are due to the peritoneal exudate and include damage to surrounding structures such as the spleen, intestines and major blood vessels. Jaundice due to local oedema or an associated gallstone is not uncommon. Pancreatic ascites may develop owing to rupture of a pancreatic duct or pseudocyst, and is characterized by an exudate with a high amylase content.

The later complications of pancreatitis have been well described by Trapnell (1971) and include abscess, pseudocyst, haematemesis, duodenal obstruction and colonic necrosis (Katz et al., 1974).

In the early stages of the disease the clinician is faced with the difficulty of recognizing the patient with incipient or established haemorrhagic or necrotizing pancreatitis. Continuing severe pain, shock, cyanosis, paralytic ileus, toxaemia, respiratory and renal failure all suggest severe underlying pancreatitis. Prolongation of the ileus was considered by Trapnell (1966) to be a particularly ominous clinical sign, as was the later development of Grey-Turner's sign. The laboratory investigations of a high WBC, low serum calcium and arterial Po_2 and a high serum methaemalbumin will also indicate fulminating pancreatitis.

Management

The mortality of acute pancreatitis has fallen since the turn of the century, but there has not been a major improvement in recent years. Specific treatment is not available and improvement in outcome has been due to an understanding and correction of the associated systemic derangements that arise. Many forms of drug treatment have been used, but there are constantly recurring problems in their assessment. First, it is impossible to extrapolate the experimental animal responses to the human situation, and secondly the variable clinical course of pancreatitis makes controlled trials difficult.

Systemic treatment

1. *Shock*: The shock state in pancreatitis is comparable to that in a large burn, but, unlike that situation, there is no rapid way of calculating fluid replacement. Losses of up to 40 per cent of the circulating blood volume may occur and replacement therapy must be closely controlled by central venous pressure, blood pressure, urine output, haematocrit and electrolytes. Large volumes of fluid, electrolytes, plasma expanders and blood may be required. The adequacy of fluid replacement is of critical importance in overcoming the early mortality (Kune, 1968a). Despite active treatment a refractory state of shock may supervene, suggesting that vasoactive substances are contributing to the response.
2. *Renal failure*: Oliguric renal failure should be treated by restoration of the circulating volume and, if necessary, by dialysis. Peritoneal dialysis is particularly effective (Wall, 1965), presumably because of the added effect of the peritoneal lavage; haemodialysis is more efficient, but there are the attendant risks of electrolyte disequilibration and haemorrhage due to the heparin in these sick patients (Gordon and Calne, 1972).
3. *Cardiorespiratory failure*: Increasing respiratory difficulties, cyanosis or psychosis should be assessed promptly by repeated measurement of arterial blood gases. Oxygen at high flows should be commenced (Ranson et al., 1973), and in extreme cases of respiratory failure and hypoxia, tracheostomy and positive pressure respiration are indicated (Louw et al., 1967). Salt-poor albumin and intensive diuretic therapy may also help to improve arterial P_{O_2} (Kellum et al., 1972). Cardiac insufficiency, indicated by a rising venous pressure and poor organ perfusion, requires digitalization and possibly isoprenaline (Louw et al., 1967). Pleural effusions should be tapped.
4. *Metabolic*: Hypocalcaemia is treated with 10 per cent calcium gluconate given intravenously, and hypomagnesaemia is treated with 25 per cent magnesium sulphate by intramuscular injection.
5. *Diabetes*: Occasionally an acute transient hyperglycaemia develops. This usually subsides without insulin which is only indicated in persistent hyperglycaemia or ketosis.

Local non-surgical treatment

The principles in treating the pancreas are to promote pancreatic blood flow (and hence reduce the incidence of early necrosis), to suppress pancreatic secretion (and thus reduce further enzymatic damage), to counteract vasoactive enzymes produced by the pancreas and to combat local infective changes.

1. *Promotion of pancreatic blood flow*: There is strong experimental evidence that promoting pancreatic blood flow will reduce the severity of pancreatitis (Goodhead, 1969a). Low molecular weight dextran has been recommended to prevent occlusion within the pancreatic microcirculation (Carey, 1970; Goodhead, 1969b), but other authors have suggested that local oedema and ascites are increased by this therapy (Anderson and Lewis, 1965). However, these latter studies did show experimental improvement with dextran 75 000. Heparin and fibrinolysin have also been used experimentally in dogs to promote blood flow in pancreatitis, with improved results (Wright and Goodhead, 1970). However, careful assessment must be made before they are accepted as therapy in the human situation, where anticoagulants must be used with caution in situations of intra-abdominal inflammation.

Adrenocortical steroids have been advocated in the treatment of acute pancreatitis (Kaplan et al., 1964) and they may act by promoting pancreatic blood flow. However, other authors have not found benefit (Kune, 1968a), and the fact that steroids may induce pancreatitis (Nelp, 1961) makes their use in therapy somewhat illogical. There are no properly controlled trials to prove the point either way and it appears that most clinicians reserve steroids for cases in extremis.

2. *Suppression of pancreatic secretion*: There is little information available on the degree of secretion taking place during an attack of pancreatitis, but it seems logical to suppress secretion if possible. Several methods have been used, including nasogastric suction, anticholinergics, acetazolamide, propylthiouracil and recently glucagon (Knight et al., 1971). None of these treatments has been shown to be of value. Anticholinergics did not have benefit in Trapnell's uncontrolled series (Trapnell, 1966), and although glucagon looks promising from a recent report (Condon et al., 1973), with a low mortality of 2 deaths in the 30 patients treated, the significance of these figures cannot be assessed because it is not known whether patients were in their first or subsequent attacks and this is known to affect the outcome (Trapnell, 1966).
3. *Inhibition of vasoactive enzymes*: Aprotinin (Trasylol) has been used for many years in the treatment of acute pancreatitis; it works as a trypsin and kallikrein inhibitor and in experimental preparations can ameliorate attacks of acute pancreatitis (Kune, 1968b). In clinical practice there has been less convincing evidence of its efficacy, possibly because of low dose and delay in commencing treatment. Early controlled trials with small numbers of patients failed to show any benefit from the drug (Skyring et al., 1965; Baden et al., 1969), but many other reports based on clinical impressions suggested that improvement was obtained. There has been a recent report of a strictly controlled double blind trial with Trasylol (Trapnell et al., 1974), using an initial dose of 200 000 units and then 200 000 units 6-hourly intravenously for 5 days. The patients admitted to

this trial either did not have an overt cause of their pancreatitis or were known to have gallbladder disease. There was a significant reduction in mortality in the 53 patients receiving the drug (4 deaths, 7·5 per cent) compared with the 52 patients receiving the placebo (13 deaths, 25 per cent), and in particular the high mortality in elderly patients was reduced. This work has reawakened the waning surgical interest in Trasylol and is of further value in that the authors have classified the severity of illness of their patients with pancreatitis by careful criteria which should serve as a model for any future clinical trials of drug therapy.

4. *Infection*: The value of prophylactic antibiotics in the early treatment of fulminating pancreatitis is open to question. There are impressions from some authors that septic complications are reduced by broad spectrum antibiotics (Louw et al., 1967; Kune, 1968a), but it appears that the outcome of the attack is not affected by this therapy (Trapnell, 1966).

Surgical treatment

The traditional view of surgical intervention in acute pancreatitis was that it should be avoided (Bowers, 1956; Thompson and Derrick, 1957), but recently there has been a trend to a more active surgical approach. The accepted indications for laparotomy are in cases of diagnostic uncertainty and pancreatic trauma. In these situations the surgeon's duty is clear. What is not so clear is the timing of laparotomy in 'proved' pancreatitis which is failing to respond to non-operative treatment, and the right course to pursue when the abdomen has been opened. Some authors (Anderson, 1965; Zimberg, 1968) have recommended surgery after 6–12 hours, if the patient has failed to improve, but extended the time to 24 hours if an underlying biliary tract condition is suspected. It remains to be seen whether this more active approach is the correct one, but there is certainly no evidence from the literature that early laparotomy is harmful (Trapnell, 1966; Louw et al., 1967; Kune, 1968a; Diaco et al., 1969). However, the incidence of burst abdomen is high—9 per cent in Trapnell's (1972) series.

If laparotomy has been performed the policy followed will depend on the findings. In cases of necrotizing pancreatitis the sloughing retroperitoneal mass should be sucked out and drained adequately. The splenic and hepatic flexures should be mobilized as there may be a retroperitoneal extension of the slough behind the colon and also into the root of the small bowel mesentery. Total pancreatectomy would be logical in severe haemorrhagic pancreatitis with its high mortality and has been carried out with success (Watts, 1963), but this prospect will daunt most surgeons and will be impossible when there is total necrosis. If haemorrhagic pancreatitis is discovered peritoneal lavage and effective sump drainage should be instituted (Waterman et al., 1968). There are sound theoretical reasons for removing the peritoneal exudate and continuing with postoperative peritoneal lavage. The experimental and clinical evidence in favour of lavage has recently been presented (Rosato et al., 1973). Peritoneal lavage can be performed in the non-operative case by the percutaneous placement of catheters, and this has been strongly recommended (Bolooki and Gliedman, 1968). The addition of Trasylol to the lavage fluid may be helpful (Wall, 1965), whilst hypothermic lavage has its advocates (Rasmussen, 1967). The final assessment of the value of these therapies must await adequate clinical trials.

The management of the infected and obstructed biliary tract associated with acute pancreatitis is uncertain; the evidence is unconvincing for or against cholecystectomy or early decompression by cholecystostomy or T-tube drainage of the bile duct. Decompression by cholecystostomy is simple and safe but the presence of stones within the duct coupled with jaundice may call for exploration and T-tube drainage. An early direct approach to a stone impacted at the ampulla of Vater is not recommended (Anderson, 1965; Louw et al., 1967; Trapnell, 1972) because of the technical problems and possibility of causing further pancreatic damage. However, Salzmann and Bartlett (1963) reported 6 patients who were successfully treated by transduodenal sphincterotomy during intractable attacks of acute pancreatitis, and so there may be a place for this operation on occasions. However, there is no question of the need for surgery in the later complications of abscess and duodenal obstruction (Trapnell, 1971). Although pseudocysts do resolve spontaneously, surgical drainage is usually indicated and this subject has been reviewed by Simpson and Srivastava (1973).

Conclusion

Until there is a fuller understanding of the pathogenesis of acute pancreatitis a rational prophylactic and therapeutic regimen cannot be instigated. At present there is little evidence in favour of the various drugs and operations recommended. In future all treatments should be scientifically assessed before gaining acceptance, and it is encouraging that multicentre trials organized on a national scale are under way in the United Kingdom.

Acknowledgements

I should like to thank Professor H. A. F. Dudley and Mr J. Trapnell for their helpful advice in the preparation of this manuscript.

References

ANDERSON M. C. (1961) Pancreatic hemorrhage. *Arch. Surg.* **83**, 467–474.

ANDERSON M. C. (1963) Venous stasis in the transition of edematous pancreatitis to necrosis. *JAMA* **183**, 534–538.

ANDERSON M. C. (1965) Surgical intervention in acute pancreatitis. *Surg. Gynecol. Obstet.* **120**, 1301–1302.

ANDERSON M. C. and LEWIS M. B. (1965) Low-molecular-weight Dextran therapy in experimental pancreatitis. *JAMA* **192**, 398–400.

ANDERSON M. C. and SCHILLER W. R. (1968) Microcirculatory dynamics in the normal and inflamed pancreas. *Am. J. Surg.* **115**, 118–127.

AVIOLI L. V., BIRGE S. J., SCOTT S. and SHIEBER W. (1969) Role of the thyroid gland during glucagon-induced hypocalcemia in the dog. *Am. J. Physiol.* **216**, 939–945.

BADEN H., JORDAL K., LUND F. and ZACHARIAE F. (1969) Prophylactic and curative action of Trasylol in pancreatitis. A double-blind trial. *Scand. J. Gastroenterol.* 4, 291–295.

BANKS P. A. (1971) Acute pancreatitis. *Gastroenterology* **61**, 382–397.

BANKS P. A. and JANOWITZ H. D. (1969) Some metabolic aspects of exocrine pancreatic disease. *Gastroenterology* **56**, 601–617.

BARRACLOUGH B. H. and COUPLAND G. A. E. (1972) Acute pancreatitis: a review. *Aust. NZ J. Surg.* **41**, 211–218.

BATTERSBY C. and GREEN M. K. (1971) The surgical significance of methaemalbuminaemia. *Gut* **12**, 995–1000.

BLAISDELL F. W. and SCHLOBOHM R. M. (1973) The respiratory distress syndrome: a review. *Surgery* **74**, 215–262.

BOLOOKI H. and GLIEDMAN M. L. (1968) Peritoneal dialysis in treatment of acute pancreatitis. *Surgery* **64**, 466–471.

BOWERS R. F. (1956) Diseases of the pancreas. *Arch. Surg.* **72**, 210–217.

CAREY L. C. (1970) Low-molecular-weight Dextran in experimental pancreatitis. *Am. J. Surg.* **119**, 197–199.

CONDON J. R., KNIGHT M. and DAY J. L. (1973) Glucagon therapy in acute pancreatitis. *Br. J. Surg.* **60**, 509–511.

COTTON P. B., SALMON P. R., BLUMGART C. H., BURWOOD R. J., DAVIES G. T., LAWRIE B. W., PIERCE J. W. and READ A. E. (1972) Cannulation of papilla of Vater via fiber-duodenoscope. *Lancet* **1**, 53–58.

CREUTZFELDT W. and SCHMIDT H. (1970) Aetiology and pathogenesis of pancreatitis. *Scand. J. Gastroenterol.* **5**, *Suppl.* 6, 47–62.

DARLE N., EKHOLM R. and EDLUND Y. (1970) Ultrastructure of the rat exocrine pancreas after long term intake of ethanol. *Gastroenterology* **58**, 62–72.

DIACO J. F., MILLER L. D. and COPELAND E. M. (1969) The role of early diagnostic laparotomy in acute pancreatitis. *Surg. Gynecol. Obstet.* **129**, 263–269.

GAMKLOU R. and EDLUND Y. (1966) Acute alcoholic pancreatitis in the rat. *Scand. J. Gastroenterol.* 1, 75–78.

GEOKAS M. C. (1972) Acute pancreatitis. *Calif. Med.* **117**, 25–39.

GEOKAS M. C., RINDERKNECHT H., SWANSON V. and HAVERBACK B. (1968) The role of elastase in acute haemorrhagic pancreatitis in man. *Lab. Invest.* **19**, 235–239.

GILLESPIE W. J. (1973) Observations on acute pancreatitis. *Br. J. Surg.* **60**, 63–65.

GLAZER G. and BENNETT A. (1974) Elevation of prostaglandin-like activity in the blood and peritoneal exudate of dogs with acute pancreatitis. *Br. J. Surg.* **61**, 922.

GLIEDMAN M. L., BOLOOKI H. and ROSEN R. G. (1970) Acute pancreatitis. *Curr. Probl. Surg.* Aug., pp. 16–19.

GOODHEAD B. (1969a) Vascular factors in the pathogenesis of acute haemorrhagic pancreatitis. *Ann. R. Coll. Surg. Engl.* **45**, 80–97.

GOODHEAD B. (1969b) Acute pancreatitis and pancreatic blood flow. *Surg. Gynecol. Obstet.* **129**, 331–340.

GORDON D. and CALNE R. Y. (1972) Renal failure in acute pancreatitis. *Br. Med. J.* **3**, 801–802.

HERMON-TAYLOR J. (1972) The exocrine pancreas. In: IRVINE W. T. (ed.) *The Scientific Basis of Surgery*, 2nd ed. Edinburgh, Churchill Livingstone, pp. 137–157.

JONES S. A., STEEDMAN R. A., KELLER T. B. and SMITH L. L. (1969) Transduodenal sphincteroplasty (not sphincterotomy) for biliary and pancreatic disease. *Am. J. Surg.* **118**, 292–306.

KALANT H. (1969) Alcohol, pancreatic secretion and pancreatitis. *Gastroenterology* **56**, 380–385.

KAPLAN M. H., COTLAR A. M. and STAGG S. J. (1964) Acute pancreatitis. Six year survey with evaluation of steroid therapy. *Am. J. Surg.* **108**, 24–30.

KATZ P., DORMAN M. J. and AUFSES A. H. (1974) Colonic necrosis complicating postoperative pancreatitis. *Ann. Surg.* **179**, 403–405.

KELLUM J. M., DEMEESTER T. R., ELKINS R. C. and ZUIDEMA G. D. (1972) Respiratory insufficiency secondary to acute pancreatitis. *Ann. Surg.* **175**, 657–662.

KNIGHT M. J., CONDON J. R. and SMITH R. (1971) Possible use of glucagon in the treatment of pancreatitis. *Br. Med. J.* **2**, 440–442.

KONOK G. P. and THOMPSON A. G. (1969) Pancreatic ductal mucosa as a protective barrier in the pathogenesis of pancreatitis. *Am. J. Surg.* **117**, 18–23.

KUNE G. A. (1968a) The challenge of severe acute pancreatitis. *Med. J. Aust.* **2**, 8–12.

KUNE G. A. (1968b) The treatment of experimentally induced acute pancreatitis. *Aust. NZ J. Surg.* **38**, 150–153.

LEVITT M. D., RAPOPORT M. and COOPERBAND S. R. (1969) The renal clearance of amylase in renal insufficiency, acute pancreatitis and macroamylasemia. *Ann. Intern. Med.* **71**, 919–925.

LOUW J. H., MARKS I. N. and BANKS S. (1967) The management of severe acute pancreatitis. *Postgrad. Med. J.* **43**, 31–44.

MCCUTCHEON A. D. (1968) A fresh approach to the pathogenesis of pancreatitis. *Gut* **9**, 296–310.

MESZAROS I., GOTH L. and VATTAY GY. (1973) The value of serum catalase activity determinations in acute pancreatitis. *Am. J. Dig. Dis.* **18**, 1035–1041.

MORGAN A., ROBINSON L. A. and WHITE T. T. (1968) Postoperative changes in the trypsin inhibitor activities of human pancreatic juice and the influence of infusion of Trasylol on the inhibitor activity. *Am. J. Surg.* **115**, 131–139.

MORGAN A. P., JENNY M. E. and HAESSLER H. (1965) Phospholipids, acute pancreatitis and the lungs; effect of lecithinase infusion on pulmonary surface activity in dogs. *Ann. Surg.* **167**, 329–335.

MULDOWNEY F. P., MCKENNA T. J., KYLE L. H., FREANEY R. and SWAN M. (1970) Parathormone-like effect of magnesium replenishment in steatorrhea. *New Engl. J. Med.* **282**, 61–68.

NANCE F. C. and CAIN J. L. (1968) Studies of hemorrhagic pancreatitis in germ free dogs. *Gastroenterology* **55**, 368–374.

NELP W. B. (1961) Acute pancreatitis associated with steroid therapy. *Arch. Intern. Med.* **108**, 702–710.

OFSTAD E. (1970) Formation and destruction of plasma kinins during experimental acute haemorrhagic pancreatitis in dogs. *Scand. J. Gastroenterol.* **5**, *Suppl.* 5, 9–44.

OFSTAD E., AMUNDSEN E., HAGEN P. O. (1969) Experimental acute pancreatitis in dogs. Histamine release induced by pancreatic exudate. *Scand. J. Gastroenterol.* **4**, 75–79.

ORREGO-MATTE H., NAVIA E., FERES A. and COSTA-MAILLERE L. (1969) Ethanol ingestion and incorporation of ^{32}P into phospholipids of pancreas in the rat. *Gastroenterology* **56**, 280–285.

PFEFFER R. B., STASIOR O. and HINTON J. W. (1957) The clinical picture of the sequential development of acute hemorrhagic pancreatitis in the dog. *Surg. Forum* **8**, 248–251.

PIROLA R. C. and DAVIS A. E. (1968) Effect of ethyl alcohol on sphincteric resistance at the choledocho-duodenal junction in man. *Gut* **9**, 557–560.

POLLOCK A. V. (1959) Acute pancreatitis—a review of one hundred cases. *Br. Med. J.* **1**, 6–10.

RANSON J. H. C., ROSES D. F. and FINK S. D. (1973) Early respiratory insufficiency in acute pancreatitis. *Ann. Surg.* **178**, 75–79.

RASMUSSEN B. L. (1967) Hypothermia peritoneal dialysis in the treatment of acute hemolytic pancreatitis. *Am. J. Surg.* **114**, 716–721.

REID I. C., PAULETTE R. E., CHALLIS T. W. and HINTON J. W. (1958) The mechanism of the pathogenesis of pancreatic necrosis and the therapeutic effect of propylthiouracil. *Surgery* **43**, 538–549.

ROSATO E. F., COWAN R. P. and ROSATO F. E. (1970) Duodenal pressure as a factor in the cause of pancreatitis. *Surgery* **68**, 837–841.

ROSATO E. F., MULLIS F. W. and ROSATO F. E. (1973) Peritoneal lavage therapy in hemorrhagic pancreatitis. *Surgery* **74**, 106–115.

SALZMAN E. W. and BARTLETT M. K. (1963) Pancreatic duct exploration in selected cases of acute pancreatitis. *Ann. Surg.* **158**, 859–863.

SCHAPIRO H., WRUBLE L. D. and BRITT L. G. (1966) The possible mechanism of alcohol in the production of acute pancreatitis. *Surgery* **60**, 1108–1111.

SCHMIDT H. and CREUTZFELDT W. (1969) The possible role of phospholipase A in the pathogenesis of acute pancreatitis. *Scand. J. Gastroenterol.* **4**, 39–48.

SIMPSON A. and SRIVASTAVA V. K. (1973) Pseudocyst of the pancreas. *Br. J. Surg.* **60**, 40–45.

SKYRING A., SINGER A. and TORNYA P. (1965) Treatment of acute pancreatitis with Trasylol: report of a controlled therapeutic trial. *Br. Med. J.* **2**, 627–629.

SONG H., TIETZ N. W. and TAN C. (1970) Usefulness of serum lipase, esterase and amylase estimation in the diagnosis of pancreatitis—a comparison. *Clin. Chem.* **16**, 264–268.

THOMPSON J. A. and DERRICK J. R. (1957) The diagnosis and management of acute pancreatitis. *Am. J. Surg.* **94**, 558–563.

TRAPNELL J. E. (1966) The natural history and prognosis of acute pancreatitis. *Ann. R. Coll. Surg. Engl.* **38**, 265–287.

TRAPNELL J. E. (1971) Management of the complications of acute pancreatitis. *Ann. R. Coll. Surg. Engl.* **49**, 361–372.

TRAPNELL J. E. (1972) The natural history and management of acute pancreatitis. *Clin. Gastroenterol.* **1**, 147–166.

TRAPNELL J. E., RIGBY C. C., TALBOT C. H. and DUNCAN E. H. L. (1974) A controlled trial of Trasylol in the treatment of acute pancreatitis. *Br. J. Surg.* **61**, 177–182.

WALL A. J. (1965) Peritoneal dialysis in the treatment of severe acute pancreatitis. *Med. J. Aust.* **2**, 281–283.

WALLENSTEN S. (1958) Acute pancreatitis and hyperdiastasuria after partial gastrectomy. *Acta Chir. Scand.* **115**, 182–188.

WALTON B. E., SCHAPIRO A. and WOODWARD E. R. (1962) The effect of alcohol and histamine on pancreatic secretion. *Am. Surg.* **28**, 443–444.

WATERMAN N. G., WALSKY R., KOSDAN M. L. and ABRAMS B. L. (1968) The treatment of acute haemorrhagic pancreatitis by sump drainage. *Surg. Gynecol. Obstet.* **126**, 963–971.

WATTS G. T. (1963) Total pancreatectomy for fulminant pancreatitis. *Lancet* **2**, 384.

WEINER S., GRAMATICA L., VOEGLE L. D., HAUMAN R. L. and ANDERSON M. C. (1970) Role of the lymphatic system in the pathogenesis of inflammatory disease in the biliary tract and pancreas. *Am. J. Surg.* **119**, 55–61.

WEISSMANN G. (1965) Lysosomes. *New Engl. J. Med.* **273**, 1143–1149.

WILLIAMS L. F. and BYRNE J. J. (1968) The role of bacteria in hemorrhagic pancreatitis. *Surgery* **64**, 967–972.

WINSTONE N. E. (1965) Methaemalbumin in acute pancreatitis. *Br. J. Surg.* **52**, 804–808.

WRIGHT P. W. and GOODHEAD B. (1970) Prevention of hemorrhagic pancreatitis with fibrinolysin or heparin. *Arch. Surg.* **100**, 42–46.

ZIEVE L. and VOGEL W. C. (1960) Measurement of lecithinase A in serum and other body fluids. *J. Lab. Clin. Med.* **57**, 586–599.

ZIMBERG Y. H. (1968) Pancreatitis: principles of management. *Surg. Clin. North Am.* **48**, 889–905.

AVIOLI L. V., BIRGE S. J., SCOTT S. and SHIEBER W. (1969) Role of the thyroid gland during glucagon-induced hypocalcemia in the dog. *Am. J. Physiol.* **216**, 939–945.

BADEN H., JORDAL K., LUND F. and ZACHARIAE F. (1969) Prophylactic and curative action of Trasylol in pancreatitis. A double-blind trial. *Scand. J. Gastroenterol.* 4, 291–295.

BANKS P. A. (1971) Acute pancreatitis. *Gastroenterology* **61**, 382–397.

BANKS P. A. and JANOWITZ H. D. (1969) Some metabolic aspects of exocrine pancreatic disease. *Gastroenterology* **56**, 601–617.

BARRACLOUGH B. H. and COUPLAND G. A. E. (1972) Acute pancreatitis: a review. *Aust. NZ J. Surg.* **41**, 211–218.

BATTERSBY C. and GREEN M. K. (1971) The surgical significance of methaemalbuminaemia. *Gut* **12**, 995–1000.

BLAISDELL F. W. and SCHLOBOHM R. M. (1973) The respiratory distress syndrome: a review. *Surgery* **74**, 215–262.

BOLOOKI H. and GLIEDMAN M. L. (1968) Peritoneal dialysis in treatment of acute pancreatitis. *Surgery* **64**, 466–471.

BOWERS R. F. (1956) Diseases of the pancreas. *Arch. Surg.* **72**, 210–217.

CAREY L. C. (1970) Low-molecular-weight Dextran in experimental pancreatitis. *Am. J. Surg.* **119**, 197–199.

CONDON J. R., KNIGHT M. and DAY J. L. (1973) Glucagon therapy in acute pancreatitis. *Br. J. Surg.* **60**, 509–511.

COTTON P. B., SALMON P. R., BLUMGART C. H., BURWOOD R. J., DAVIES G. T., LAWRIE B. W., PIERCE J. W. and READ A. E. (1972) Cannulation of papilla of Vater via fiber-duodenoscope. *Lancet* **1**, 53–58.

CREUTZFELDT W. and SCHMIDT H. (1970) Aetiology and pathogenesis of pancreatitis. *Scand. J. Gastroenterol.* **5**, *Suppl.* 6, 47–62.

DARLE N., EKHOLM R. and EDLUND Y. (1970) Ultrastructure of the rat exocrine pancreas after long term intake of ethanol. *Gastroenterology* **58**, 62–72.

DIACO J. F., MILLER L. D. and COPELAND E. M. (1969) The role of early diagnostic laparotomy in acute pancreatitis. *Surg. Gynecol. Obstet.* **129**, 263–269.

GAMKLOU R. and EDLUND Y. (1966) Acute alcoholic pancreatitis in the rat. *Scand. J. Gastroenterol.* **1**, 75–78.

GEOKAS M. C. (1972) Acute pancreatitis. *Calif. Med.* **117**, 25–39.

GEOKAS M. C., RINDERKNECHT H., SWANSON V. and HAVERBACK B. (1968) The role of elastase in acute haemorrhagic pancreatitis in man. *Lab. Invest.* **19**, 235–239.

GILLESPIE W. J. (1973) Observations on acute pancreatitis. *Br. J. Surg.* **60**, 63–65.

GLAZER G. and BENNETT A. (1974) Elevation of prostaglandin-like activity in the blood and peritoneal exudate of dogs with acute pancreatitis. *Br. J. Surg.* **61**, 922.

GLIEDMAN M. L., BOLOOKI H. and ROSEN R. G. (1970) Acute pancreatitis. *Curr. Probl. Surg.* Aug., pp. 16–19.

GOODHEAD B. (1969a) Vascular factors in the pathogenesis of acute haemorrhagic pancreatitis. *Ann. R. Coll. Surg. Engl.* **45**, 80–97.

GOODHEAD B. (1969b) Acute pancreatitis and pancreatic blood flow. *Surg. Gynecol. Obstet.* **129**, 331–340.

GORDON D. and CALNE R. Y. (1972) Renal failure in acute pancreatitis. *Br. Med. J.* **3**, 801–802.

HERMON-TAYLOR J. (1972) The exocrine pancreas. In: IRVINE W. T. (ed.) *The Scientific Basis of Surgery*, 2nd ed. Edinburgh, Churchill Livingstone, pp. 137–157.

JONES S. A., STEEDMAN R. A., KELLER T. B. and SMITH L. L. (1969) Transduodenal sphincteroplasty (not sphincterotomy) for biliary and pancreatic disease. *Am. J. Surg.* **118**, 292–306.

KALANT H. (1969) Alcohol, pancreatic secretion and pancreatitis. *Gastroenterology* **56**, 380–385.

KAPLAN M. H., COTLAR A. M. and STAGG S. J. (1964) Acute pancreatitis. Six year survey with evaluation of steroid therapy. *Am. J. Surg.* **108**, 24–30.

KATZ P., DORMAN M. J. and AUFSES A. H. (1974) Colonic necrosis complicating postoperative pancreatitis. *Ann. Surg.* **179**, 403–405.

KELLUM J. M., DEMEESTER T. R., ELKINS R. C. and ZUIDEMA G. D. (1972) Respiratory insufficiency secondary to acute pancreatitis. *Ann. Surg.* **175**, 657–662.

KNIGHT M. J., CONDON J. R. and SMITH R. (1971) Possible use of glucagon in the treatment of pancreatitis. *Br. Med. J.* **2**, 440–442.

KONOK G. P. and THOMPSON A. G. (1969) Pancreatic ductal mucosa as a protective barrier in the pathogenesis of pancreatitis. *Am. J. Surg.* **117**, 18–23.

KUNE G. A. (1968a) The challenge of severe acute pancreatitis. *Med. J. Aust.* **2**, 8–12.

KUNE G. A. (1968b) The treatment of experimentally induced acute pancreatitis. *Aust. NZ J. Surg.* **38**, 150–153.

LEVITT M. D., RAPOPORT M. and COOPERBAND S. R. (1969) The renal clearance of amylase in renal insufficiency, acute pancreatitis and macroamylasemia. *Ann. Intern. Med.* **71**, 919–925.

LOUW J. H., MARKS I. N. and BANKS S. (1967) The management of severe acute pancreatitis. *Postgrad. Med. J.* **43**, 31–44.

MCCUTCHEON A. D. (1968) A fresh approach to the pathogenesis of pancreatitis. *Gut* **9**, 296–310.

MESZAROS I., GOTH L. and VATTAY GY. (1973) The value of serum catalase activity determinations in acute pancreatitis. *Am. J. Dig. Dis.* **18**, 1035–1041.

MORGAN A., ROBINSON L. A. and WHITE T. T. (1968) Postoperative changes in the trypsin inhibitor activities of human pancreatic juice and the influence of infusion of Trasylol on the inhibitor activity. *Am. J. Surg.* **115**, 131–139.

Br. J. Surg. Vol. 62 (1975) 177–181

Plasma catecholamines in severely injured patients: a prospective study on 45 patients with multiple injuries

A. JÄÄTTELÄ, A. ALHO, V. AVIKAINEN, E. KARAHARJU, J. KATAJA,
M. LAHDENSUU, P. LEPISTÖ, P. ROKKANEN AND T. TERVO*

SUMMARY

Plasma catecholamine levels were studied in 45 severely injured patients for 8 days after the trauma. Sixteen of the patients were classified as critically injured and 29 as seriously injured.

The total plasma catecholamine values of the whole group immediately after the injury were almost twice as high as the eighth day reference values and remained significantly higher than these values for 6 hours after the trauma. On admission both the plasma adrenaline and noradrenaline levels were elevated. The plasma adrenaline levels on admission correlated with the blood volume replacement which was required within the first 6 hours.

The plasma noradrenaline levels in the critically injured group were significantly higher throughout the observation period than in the seriously injured group. A corresponding difference was observed in the plasma adrenaline concentrations only during the first 12 hours.

The results showed that strong stimulation of the sympathetic nervous system occurs in severely injured patients. Factors stimulating the sympathetic nervous system apparently included hypovolaemia, tissue hypoxia, acidosis and the pain produced by the truama and therapeutic measures.

SEVERAL factors that have been found individually to cause stimulation of the sympathetic nervous system are associated with severe trauma; these include pain, fear, haemorrhage, tissue damage, etc. (Walker et al., 1959). A similar effect is exerted by the different anaesthetic procedures (Price, 1957; Black et al., 1969) and surgical interventions (Nikki et al., 1972) which are necessary in the case of severely injured patients.

Our knowledge of the total stimulation of the sympathetic nervous system caused by various factors in traumatized patients is minimal. Measurement of the sympathetic activity is difficult. The urinary catecholamine content has been considered to give a reliable overall idea of the long term activity of the sympathetic nervous system (Crout, 1961). Post-traumatic elevation of the level of urinary catecholamines and their metabolites has been established (Coward and Smith, 1966). Urinary catecholamine measurements are, however, incapable of recording the rapid variations characteristic of sympathetic activity. On the other hand, this can be done by measuring the plasma catecholamine concentrations (Carruthers et al., 1970).

The purpose of this study was to elucidate the activity of the sympathetic nervous system and the role of the factors influencing it by measuring the plasma catecholamine levels for 8 days following injury.

Patients and methods

Forty-five consecutive patients with multiple injuries who had been admitted to the intensive care unit of University Central Hospital, Helsinki, were investigated. The criterion for investigation was that the patient was admitted within 2 hours of the trauma and that the research bed was free. A traffic accident was the cause of injury in 35 cases. The patients with two or more critical injuries were graded as critically injured (*Table I*); the mortality in this group was 9 out of 16. All 29 patients survived in the group graded as seriously injured.

The main treatment for shock was compensation of hypovolaemia. Treatment was started with an infusion of 1000 ml of dextran with saline (Macrodex) and continued with balanced saline solutions up to 1000 ml and blood transfusions. No sympathomimetic or sympatholytic agents were used in the treatment of

Table I: AGE, SEX AND INJURIES OF THE PRESENT SERIES

	Critically injured group	Seriously injured group
Number of patients:	16	29
Age (yr, mean±s.e.):	39±3·8	34±2·8
Sex (male : female):	8/8	22/7

	Degree of severity*		Degree of severity	
Site of trauma	Critical	Moderate	Critical	Moderate
Thorax	8	1	2	9
Abdomen	4	3	1	2
Pelvis	6	4	2	8
Head	9	2	2	8
Spine	1	3	0	1
Upper limbs	1	4	0	5
Lower limbs	7	4	14	12
Total	36	21	21	45

* *See also* classification of Alho and Rokkanen (1973).

---

* Department of Orthopaedics and Traumatology, University Central Hospital, Helsinki, and the Department of Pharmacology, University of Helsinki, Finland.
Present address of A. Jäättelä: Second Department of Medicine, University Central Hospital, 00290 Helsinki 29, Finland.

shock. During the first 24 hours 14 patients were given 30 mg/kg of methylprednisone, divided into three doses, at intervals of 8 hours. Acidosis was corrected if necessary with 7·5 per cent sodium bicarbonate. When the patient was considered incapable of adequate respiration on the basis of the clinical status and the arterial blood gas analysis, volume-controlled respirator treatment was instituted.

Major operations were performed under nitrous oxide–oxygen relaxant anaesthesia (*Table II*). The adjuvants used when necessary were fentanyl and droperidole. Pethidine and atropine were used for premedication.

Systolic and diastolic blood pressure (by the indirect method) and heart rate were recorded at least once every hour. On admission a catheter was inserted in the superior vena cava. The central venous pressure was not always measured until 6 hours after the accident.

Blood samples for catecholamine measurements were taken through the central venous catheter at 0–2, 6, 12, 24 hours and 2 days after injury. In addition, a reference sample was taken 8 days after the accident. Samples of arterial blood were taken for the determination of pH, standard bicarbonate, BE, $P\mathrm{CO}_2$ and $P\mathrm{O}_2$ at the same time as the specimens for catecholamine determination. Among other values, the haematocrit and eosinophil levels were determined.

The material was treated by automatic data processing (Computer Centre, University of Helsinki). The t-test, χ^2 test and Fisher test were performed.

Table II: MAJOR SURGICAL PROCEDURES

Surgical procedures	Critically injured group: Within 6 hours	Critically injured group: After 6 hours	Seriously injured group: Within 6 hours	Seriously injured group: After 6 hours
Laparotomy	3	3	0	0
Thoractomy	0	2	0	1
Thoracolaparotomy	2	0	0	0
Thoracotomy or laparotomy and other procedures	1	0	3	1
Internal fixation*	2	2	6	2
Total	8	7	9	4

* The internal fixations performed within 6 hours were: 1 fixed angle nailing of the femur, 4 intramedullary nailings of the femur, 2 intramedullary nailings of the tibia and 1 plating of the dorsal spine. The later internal fixations were: 1 intramedullary nailing, 1 fixed angle nailing and 1 L-plating of the femur and 1 intramedullary nailing of the femur and tibia.

Catecholamine determinations

The technique used for the quantitative determination of adrenaline and noradrenaline in the plasma was based on the principles described by Vendsalu (1960). Each determination required an 18-ml sample of blood. Perchloric acid was used in the deproteinization of the plasma. Dowex 50-X4 columns (200–400 mesh, dimensions 28 mm² × 20 mm) in hydrogen form were used for purification of the extracts. The elution was performed with N hydrochloric acid. The adrenaline and noradrenaline in the eluate were determined spectrophotofluorometrically (Aminco-Bowman) after oxidation with potassium ferrocyanide and subsequent rearrangement to adrenolutine and noradrenolutine. The fluorescences of the lutines of adrenaline and noradrenaline were measured at different wavelengths. Faded blanks and reagent blanks were calculated as described by Vendsalu (1960). Internal standards were used by adding known amounts of adrenaline or noradrenaline or both to the plasma samples. Recovery by the method was 78 ± 4 (mean ± s.e.) per cent of adrenaline and 73 ± 4 per cent of noradrenaline. Duplicate extractions on plasma samples gave results that varied no more than 10 per cent.

Results

The means of the systolic blood pressure, heart rate, haematocrit and the cumulative volume compensation for the whole series at the corresponding intervals are presented in *Table III*. On admission the arterial pH (7·34 ± 0·01), standard bicarbonate (19·4 ± 0·6 mmol/l) and $P\mathrm{CO}_2$ (35·4 ± 1·1 mm Hg) values showed a tendency towards metabolic acidosis which had been corrected by 6 hours. The $P\mathrm{O}_2$ was below 75 mm Hg on admission in 17 patients, at 6 hours in 10 patients and at 12 hours in 6 patients.

The means of the total plasma catecholamine, adrenaline and noradrenaline levels for the whole series are shown in *Fig.* 1. The highest value of the total plasma catecholamines (2·03 ± 0·33 μg/l) was recorded on admission. It was significantly higher ($P < 0·001$) than the 8-day value (1·09 ± 0·09 μg/l). Subsequently, the total plasma catecholamine level fell evenly and did not differ significantly ($P < 0·02$) from the reference value except at 6 hours. The plasma adrenaline content was highest on admission (0·95 ± 0·28 μg/l), had dropped to 0·61 ± 0·18 μg/l by 6 hours and the reference value at 8 days was 0·38 ± 0·06 μg/l. The noradrenaline content both on admission (1·08 ± 0·12 μg/l) and at 6 hours (1·14 ± 0·16 μg/l)

Table III: SYSTOLIC BLOOD PRESSURE, HEART RATE, HAEMATOCRIT AND THE CUMULATIVE BLOOD VOLUME REPLACEMENT AFTER INJURY

Time interval from accident	Systolic blood pressure (mm Hg)	Heart rate (per minute)	Haematocrit	Volume compensation (litres)
Admission	95±6	107±3	—	—
2 Hours	120±6	106±3	0·40±0·01	1·0±0·2
6 Hours	128±3	110±3	—	4·0±0·5
12 Hours	129±3	103±4	0·36±0·01	4·8±0·5
24 Hours	131±5	106±3	0·35±0·01	5·6±0·6
2 Days	143±4	100±3	0·33±0·01	—
8 Days	141±4	102±3	0·38±0·01	—

Results given as means ± s.e.

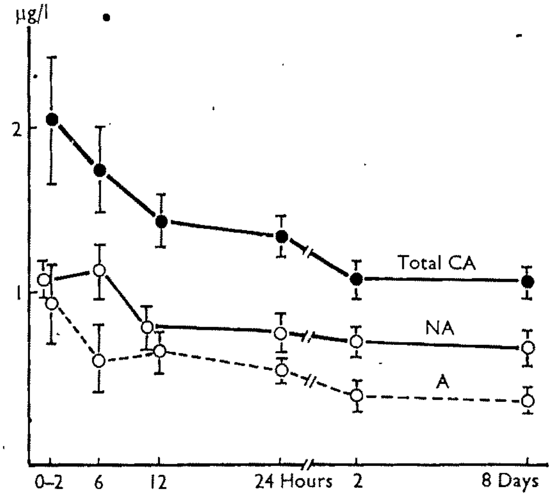


Fig. 1. Total plasma catecholamines (total CA), adrenaline (A) and noradrenaline (NA) of the whole series at different times after injury (mean and s.e.).

was significantly higher ($P<0{\cdot}02$ and $P<0{\cdot}05$ respectively) than the reference value (0·71 ± 0·09 µg/l).

On admission the mean systolic blood pressure in the critically injured group was 78 ± 10 mm Hg and in the seriously injured group 105 ± 7 mm Hg ($P<0{\cdot}02$). At 6 hours the corresponding values were 123 ± 9 mm Hg and 130 ± 6 mm Hg and the difference between the groups had thus disappeared. The mean heart rate value on admission in the critically injured group was 117 ± 4/minute and in the seriously injured group 102 ± 4/minute ($P<0{\cdot}01$). After 48 hours no differences in blood pressure or heart rate were recorded between the groups.

The volumes of blood given to the critically and the severely injured in the course of the first 24 hours are shown in *Fig.* 2. The amount of blood (6·2 ± 0·9 litres) given to the critically injured during the first 6 hours was significantly greater ($P<0{\cdot}001$) than that (2·7 ± 0·4 litres) received by the severely injured.

There were no significant differences in the haematocrit values or the central venous pressures between the

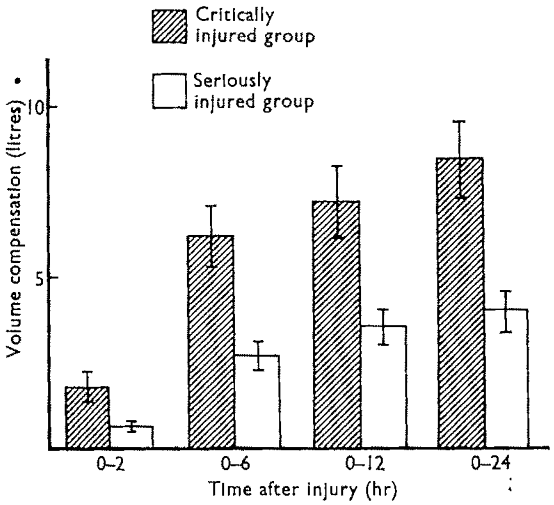


Fig. 2. Cumulative compensation of hypovolaemia in the critically injured and seriously injured groups during the first 24 hours after injury (mean and s.e.).

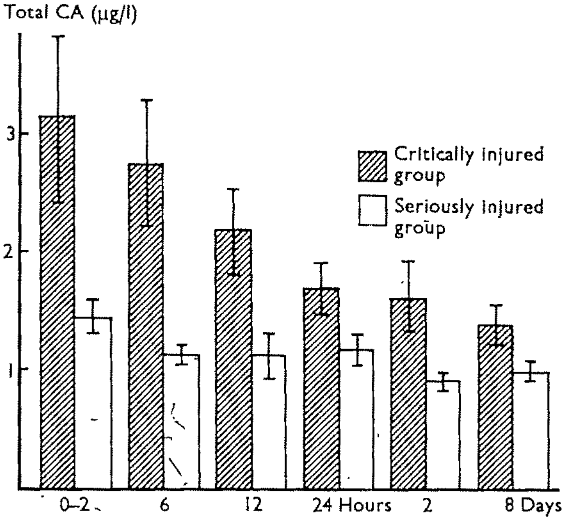


Fig. 3. Total plasma catecholamines (total CA) in the critically injured and seriously injured groups at different times after injury (mean and s.e.).

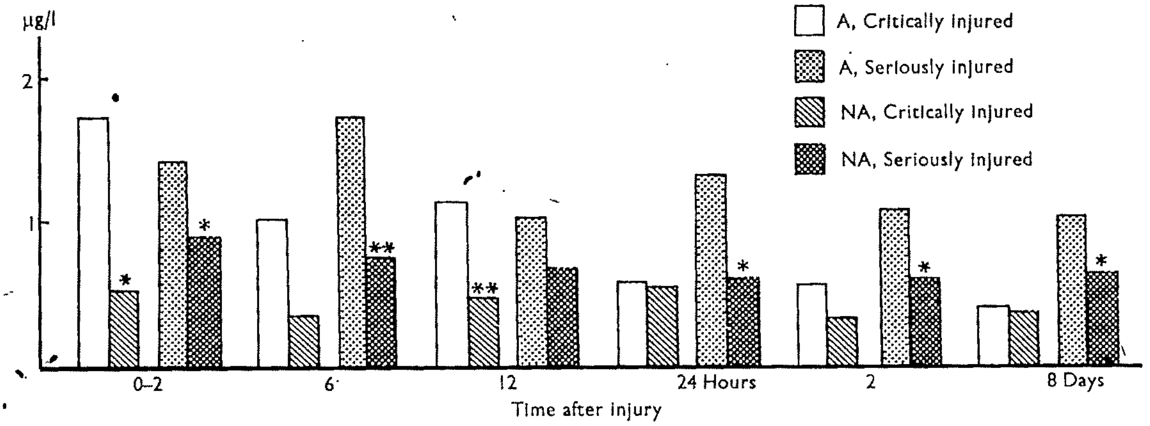


Fig. 4. Plasma adrenaline (A) and noradrenaline (NA) in the critically injured and seriously injured groups at different times after injury (mean and s.e.). * $P<0{\cdot}05$. ** $P<0{\cdot}01$.

groups. On admission metabolic acidosis was more pronounced in the critically than in the seriously injured group. During treatment this difference disappeared at 12 hours. On admission Po_2 was below 75 mm Hg in 8 critically injured patients and in 9 patients of the seriously injured group.

The total plasma catecholamine level on admission was 3·14 ± 0·83 μg/l in the critically injured group and 1·43 ± 0·12 μg/l in the seriously injured group ($P < 0·01$) (*Fig.* 3). The difference between the total catecholamines of the groups later decreased evenly but was statistically significant throughout the 8-day period. The adrenaline and noradrenaline contents of the plasma were similarly significantly higher ($P < 0·05$) on admission in the critically than in the severely injured group (*Fig.* 4). There were no significant inter-group differences in the adrenaline levels after 12 hours ($P < 0·01$), but the differences in the noradrenaline levels persisted.

The blood volume transfused within the first 6 hours correlated with the plasma adrenaline levels recorded on admission ($P < 0·05$). No corresponding correlation was established for noradrenaline.

The plasma catecholamine levels of the patients given methylprednisone did not differ from those of the patients not given this drug. Patients receiving no methylprednisone showed no correlation between the eosinophil cell count and plasma catecholamine level.

The plasma adrenaline levels of 9 patients who died from their injuries were significantly higher than the levels of the survivors ($P < 0·05$). No such differences were observed in the noradrenaline levels.

Discussion

'Many attempts have been made to measure adrenaline and noradrenaline levels in blood after injury but no consistent changes have been detected' (Johnston, 1972). Differing from this conclusion, we observed in a preliminary report (Jäättelä, 1972b) and in the present study significantly elevated post-traumatic plasma catecholamine levels in patients with multiple injuries. The elevation of the plasma adrenaline concentration was of short duration, but the noradrenaline concentration at 8 days was still almost double the value recorded for healthy persons by the same method (Jäättelä, 1972a). The elevation of the plasma catecholamine levels was significantly higher in the critically injured than in the severely injured group. The main reason for the divergence of these results from earlier observations is probably the great severity of the injuries suffered by the patients in the present series.

Noradrenaline acts as a transmitter substance in the peripheral nerve endings of the sympathetic nervous system. The adrenal medulla, which is comparable functionally with sympathetic ganglions, secretes both adrenaline and noradrenaline (Axelrod and Weinshilboum, 1972). The stimulation of the sympathetic nervous system in severely injured patients is obviously produced by several factors. Animal experiments have shown that profuse blood loss alone greatly increases the plasma catecholamines (Watts, 1956; Lillehei et al., 1964). The increase is believed to take place partly via the volume receptor, pressor-receptor and chemoreceptor systems (Berne and Levy, 1967; Ganong, 1973), and partly as a result of tissue hypoxia and acidosis (Woods et al., 1956). Young and Gray (1956) found that trauma alone, without external blood loss, produced an increase in the plasma catecholamine concentrations of rat.

In the emergency treatment of severe trauma, operations under general anaesthesia are often necessary. Both the operative stress (Gött and Klensch, 1970; Nikki et al., 1972) and the different methods of anaesthesia (Price, 1957; Black et al., 1969) have been found to produce an increase in plasma catecholamines. Other therapeutic interventions, such as tracheal suction, exert a stimulating effect on the sympathetic nervous system (Jäättelä and Heinonen, 1971). Eight of 17 primary operative procedures (within 6 hours) in the present series were done for operative fixation of fractures. Of course, priority was always given to more vital injuries. Our experience is that patients with multiple injuries are easier to nurse and they feel better with their fractures stably fixed than in plaster or on traction. This may be important in diminishing the stimuli for catecholamine secretion.

In the present study the highest plasma catecholamine levels were recorded immediately after the trauma, when hypovolaemia, hypoxaemia, acidosis and pain were at their most intense. The plasma catecholamine levels during anaesthesia and operation were lower than the initial values, which shows that the catecholamine-releasing effect of these factors was slight compared with that of hypovolaemia. The fact that the plasma noradrenaline level remained higher in the critically injured than in severely injured patients at 8 days was probably due to various stress factors.

The plasma adrenaline but not the noradrenaline levels on admission correlated with the blood volume transfused within the first 6 hours. Lillehei et al. (1964) observed in their experiments with dogs that at the beginning of haemorrhage the plasma adrenaline concentration increased steeply and proportionately to the volume deficit and blood pressure fall.

The haematocrit values decreased in the whole series until the second day, despite the fact that the patients were already haemodynamically stable at the end of the first day. This is accounted for by slow haemodilution. Concurrently with this there was a decrease in catecholamine excretion, leading in turn to dilatation of the vascular bed (Simmons et al., 1969). This obviously also contributed to the decrease in the haematocrit values at 2 days.

Our findings indicate that multiple injuries in man initially produce a pronounced increase in both the adrenaline and the noradrenaline levels of plasma. This is partly attributable to the increased excretion by the adrenal medulla caused by hypovolaemia, and partly to the release of noradrenaline from the sympathetic nerve endings caused by tissue hypoxia and acidosis. After correction of these causative factors, the stimulating effect of pain and various other stress factors on the sympathetic nervous system continues, as is suggested by the persistingly high plasma noradrenaline levels, particularly in critically injured patients.

References

ALHO A. and ROKKANEN P. (1973) Recovery of patients needing intensive care for blunt injuries. *Ann. Chir. Gynaecol. Fenn.* **62**, 64–68.

AXELROD J. and WEINSHILBOUM R. (1972) Catecholamines. *New Engl. J. Med.* **287**, 237–242.

BERNE R. M. and LEVY M. N. (1967) *Cardiovascular Physiology*. St Louis, Mosby, pp. 132–169.

BLACK G. W., MCARDLE L., MCCULLOUGH H. and UNNI V. K. N. (1969) Circulating catecholamines and some cardiovascular, respiratory, metabolic and pupillary responses during diethyl ether anaesthesia. *Anaesthesia* **24**, 168–179.

CARRUTHERS M., CONWAY N., SOMMERVILLE W., TAGGART P. and BATES D. (1970) Validity of plasma catecholamine estimations. *Lancet* **2**, 62–67.

COWARD R. F. and SMITH P. (1966) Excretion of metanephrines in postoperative stress. *Clin. Chim. Acta* **14**, 832–833.

CROUT J. R. (1961) Catecholamines in urine. *Stand. Meth. Clin. Chem.* **3**, 62–80.

GANONG W. F. (1973) *Review on Medical Physiology*. Los Altos, California, Lange Medical Publications, pp. 433–442.

GÖTT U. and KLENSCH H. (1970) Plasmakatecholaminänderungen bei verschiedenen Anäesthesietechniken. In: HENSCHEL W. F. (ed.), *Neue klinische Aspekte der Neuroleptanalgesie*. New York, Schattauer, pp. 51–58.

JOHNSTON I. D. A. (1972) The endocrine response to trauma. *Adv. Clin. Chem.* **15**, 255–285.

JÄÄTTELÄ A. (1972a) Plasma catecholamines in the diagnosis and localisation of phaechromocytoma. *Ann. Clin. Res.* **4**, 78–83.

JÄÄTTELÄ A. (1972b) Effect of traumatic shock on plasma catecholamine levels in man. *Ann. Clin. Res.* **4**, 204–212.

JÄÄTTELÄ A. and HEINONEN J. (1971) Effect of tracheal suction on plasma catecholamine levels. *Scand. J. Clin. Lab. Invest.* **27**, *Suppl.* **116**, 74.

LILLEHEI R. C., LONGERBEAM J. K., BLOCH J. H. and MANAX W. G. (1964) The modern treatment of shock based on physiologic principles. *Clin. Pharmacol. Ther.* **5**, 63–101.

NIKKI P., TAKKI S., TAMMISTO T. and JÄÄTTELÄ A. (1972) Effect of operative stress on plasma catecholamine levels. *Ann. Clin. Res.* **4**, 146–151.

PRICE H. L. (1957) Circulating adrenaline and noradrenaline during diethyl ether anaesthesia in man. *Clin. Sci.* **16**, 377–387.

SIMMONS R. L., HEISTERKAMP C. A., MOSELY R. V. and DOTY D. B. (1969) Postresuscitative blood volumes in combat casualties. *Surg. Gynecol. Obstet.* **128**, 1193–1201.

VENDSALU A. (1960) Studies on adrenaline and noradrenaline in human plasma. *Acta Physiol. Scand.* **49**, *Suppl.* 173.

WALKER W. F., ZILELI M. S., REUTTER F. W., SHOEMAKER W. C., FRIEND D. and MOORE F. D. (1959) Adrenal medullary secretion in hemorrhagic shock. *Am. J. Physiol.* **197**, 773–780.

WATTS D. T. (1956) Arterial blood epinephrine levels during hemorrhagic hypotension in dogs. *Am. J. Physiol.* **184**, 271–274.

WOODS E. F., RICHARDSON J. A., RICHARDSON A. K. and BOZEMAN R. F. jun. (1956) Plasma concentrations of epinephrine and arterenol following the action of various agents on the adrenals. *J. Pharmacol. Exp. Ther.* **116**, 351–355.

YOUNG J. G. and GRAY I. (1956) Biochemical response to trauma III. Epinephrine and norepinephrine levels in plasma of rats subjected to tumbling trauma. *Am. J. Physiol.* **186**, 67–70.

stress factors on the sympathetic nervous system continues, as is suggested by the persistingly high plasma noradrenaline levels, particularly in critically injured patients.

References

ALHO A. and ROKKANEN P. (1973) Recovery of patients needing intensive care for blunt injuries. *Ann. Chir. Gynaecol. Fenn.* **62**, 64–68.

AXELROD J. and WEINSHILBOUM R. (1972) Catecholamines. *New Engl. J. Med.* **287**, 237–242.

BERNE R. M. and LEVY M. N. (1967) *Cardiovascular Physiology*. St Louis, Mosby, pp. 132–169.

BLACK G. W., MCARDLE L., MCCULLOUGH H. and UNNI V. K. N. (1969) Circulating catecholamines and some cardiovascular, respiratory, metabolic and pupillary responses during diethyl ether anaesthesia. *Anaesthesia* **24**, 168–179.

CARRUTHERS M., CONWAY N., SOMMERVILLE W., TAGGART P. and BATES D. (1970) Validity of plasma catecholamine estimations. *Lancet* **2**, 62–67.

COWARD R. F. and SMITH P. (1966) Excretion of metanephrines in postoperative stress. *Clin. Chim. Acta* **14**, 832–833.

CROUT J. R. (1961) Catecholamines in urine. *Stand. Meth. Clin. Chem.* **3**, 62–80.

GANONG W. F. (1973) *Review on Medical Physiology*. Los Altos, California, Lange Medical Publications, pp. 433–442.

GÖTT U. and KLENSCH H. (1970) Plasmakatecholaminänderungen bei verschiedenen Anäesthesietechniken. In: HENSCHEL W. F. (ed.), *Neue klinische Aspekte der Neuroleptanalgesie*. New York, Schattauer, pp. 51–58.

JOHNSTON I. D. A. (1972) The endocrine response to trauma. *Adv. Clin. Chem.* **15**, 255–285.

JÄÄTTELÄ A. (1972a) Plasma catecholamines in the diagnosis and localisation of phaechromocytoma. *Ann. Clin. Res.* **4**, 78–83.

JÄÄTTELÄ A. (1972b) Effect of traumatic shock on plasma catecholamine levels in man. *Ann. Clin. Res.* **4**, 204–212.

JÄÄTTELÄ A. and HEINONEN J. (1971) Effect of tracheal suction on plasma catecholamine levels. *Scand. J. Clin. Lab. Invest.* **27**, *Suppl.* **116**, 74.

LILLEHEI R. C., LONGERBEAM J. K., BLOCH J. H. and MANAX W. G. (1964) The modern treatment of shock based on physiologic principles. *Clin. Pharmacol. Ther.* **5**, 63–101.

NIKKI P., TAKKI S., TAMMISTO T. and JÄÄTTELÄ A. (1972) Effect of operative stress on plasma catecholamine levels. *Ann. Clin. Res.* **4**, 146–151.

PRICE H. L. (1957) Circulating adrenaline and noradrenaline during diethyl ether anaesthesia in man. *Clin. Sci.* **16**, 377–387.

SIMMONS R. L., HEISTERKAMP C. A., MOSELY R. V. and DOTY D. B. (1969) Postresuscitative blood volumes in combat casualties. *Surg. Gynecol. Obstet.* **128**, 1193–1201.

VENDSALU A. (1960) Studies on adrenaline and noradrenaline in human plasma. *Acta Physiol. Scand.* **49**, *Suppl.* 173.

WALKER W. F., ZILELI M. S., REUTTER F. W., SHOEMAKER W. C., FRIEND D. and MOORE F. D. (1959) Adrenal medullary secretion in hemorrhagic shock. *Am. J. Physiol.* **197**, 773–780.

WATTS D. T. (1956) Arterial blood epinephrine levels during hemorrhagic hypotension in dogs. *Am. J. Physiol.* **184**, 271–274.

WOODS E. F., RICHARDSON J. A., RICHARDSON A. K. and BOZEMAN R. F. jun. (1956) Plasma concentrations of epinephrine and arterenol following the action of various agents on the adrenals. *J. Pharmacol. Exp. Ther.* **116**, 351–355.

YOUNG J. G. and GRAY I. (1956) Biochemical response to trauma III. Epinephrine and norepinephrine levels in plasma of rats subjected to tumbling trauma. *Am. J. Physiol.* **186**, 67–70.

Table II: SIGNIFICANT DEEP VEIN THROMBOSIS

Age	Sex	Operation	Appearance of DVT (postop. day)	Site	Detected	Confirmed
37	M	Gastrectomy	10	Popliteal–femoral	Calf tenderness Doppler	Phlebography
39	F	Colectomy	9	Calf–femoral	Doppler	Phlebography
66	F	Colectomy	6	Calf	Calf tenderness	Phlebography
49	F	Thompson for lymphoedema	5	Calf	Calf tenderness	Phlebography
54	M	Varicose veins	7	Ileofemoral	Swelling	Doppler
55	F	Colectomy	4	Ileofemoral	Swelling	Doppler
32	F	Aortic disobliteration	7	Ileofemoral	Swelling	Doppler
42	F	Aortic disobliteration	14	Ileofemoral	Pulmonary embolus	

Table III: ILIOFEMORAL THROMBOSIS

Age	Sex	Operation	Doppler investigation		Appearance of DVT	
			Result	Day	Day	Presentation
54	M	Varicose veins	Not done		7	Swelling
55	F	Colectomy	Negative	2	4	Swelling
52	F	Aortic disobliteration	Negative	6	7	Swelling
42	F	Aortic disobliteration	Negative	9	14	Pulmonary embolus

Table IV: POSTOPERATIVE PYREXIA IN PATIENTS WITH DEEP VEIN THROMBOSIS

No pyrexia		2
Low grade pyrexia		6
Peritonitis	2	
Wound infection	1	
Bronchopneumonia	1	
No other cause	2	

these patients with varicose veins had not been examined with Doppler ultrasound, an error in view of his past history of deep vein thrombosis. Of the other 3 cases, one presented 2 days after negative Doppler examination, and in another fatal pulmonary embolism occurred on the fourteenth postoperative day. Doppler examination was normal on the ninth postoperative day and as the patient was fully ambulant no further examination was performed. In the fourth patient iliofemoral venous thrombosis of the left leg presented with gross swelling only 12 hours after a normal Doppler examination.

3. *The temperature chart*

Six of the 8 patients had low grade pyrexia in the postoperative period but most had some inflammatory focus to account for it (*Table IV*). In only 2 could it be attributed solely to the venous thrombosis. In one, calf tenderness suggested calf vein thrombosis which was confirmed by phlebography. In the second, several days' unexplained pyrexia was followed by sudden swelling of the whole of the leg (*Fig*. 2). In retrospect, this unexplained pyrexia should have been further investigated by phlebography. In 2 patients who developed deep vein thrombosis there was no postoperative pyrexia and one of these suffered a fatal pulmonary embolism (*Fig*. 3).

Discussion

This study has confirmed that Doppler ultrasound can detect thrombotic occlusions of the main vessels of the thigh and pelvis. It also confirms that in general surgical practice the patients most at risk are those over 35 years of age undergoing major abdominal operations and those with a past history of deep vein thrombosis. Screening and prophylaxis can reasonably be confined to this group.

Venous thromboses confined to the calf were not detected directly by ultrasound but 2 were detected by tenderness on Doppler examination.

In this series Doppler ultrasound has proved quite unreliable in detecting early non-occlusive iliac vein thrombosis. This situation might be improved by examining patients from the fourth postoperative day until discharge and by examining daily rather than on alternate days. However, one iliac vein thrombosis presented with leg swelling only 12 hours after a negative Doppler examination. It seems likely that these thrombi develop gradually over several days. Neither swelling nor positive Doppler findings will occur until total or near total occlusion of the vein

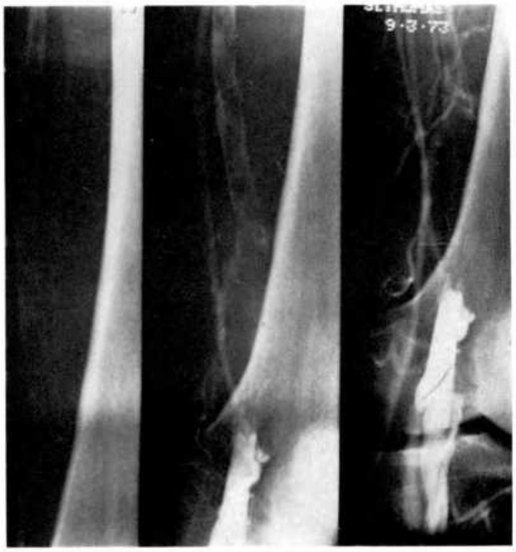


Fig. 1. Phlebogram showing femoral vein thrombosis in a 37-year-old man. This was initially detected by Doppler ultrasound.

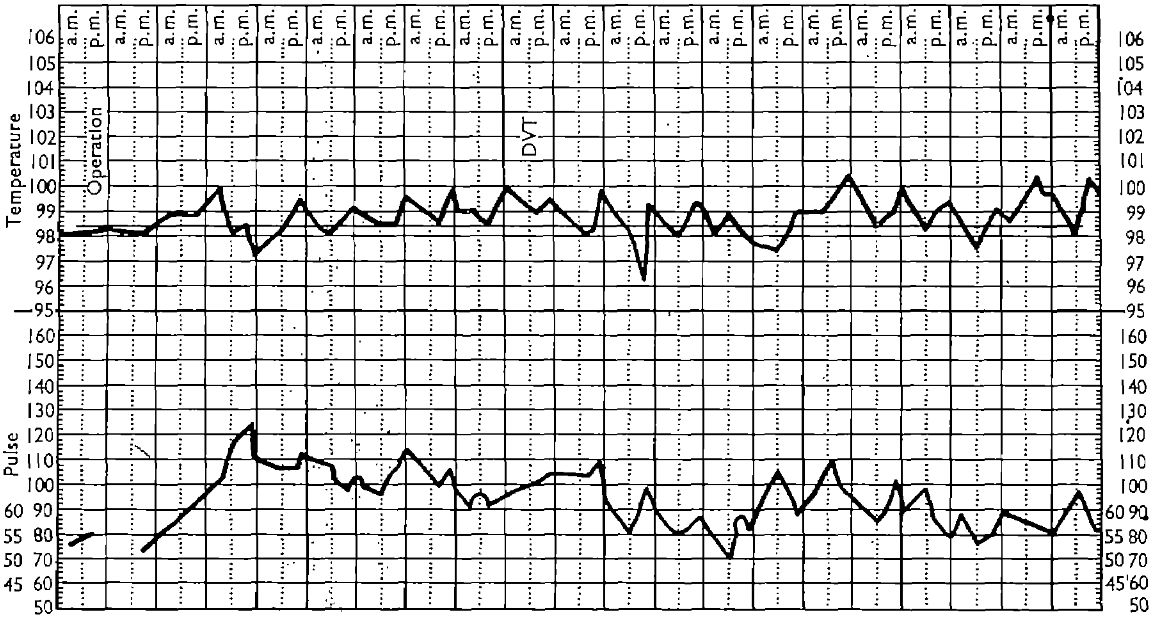


Fig. 2. Low grade pyrexia indicating early iliac vein thrombosis in a 52-year-old woman.

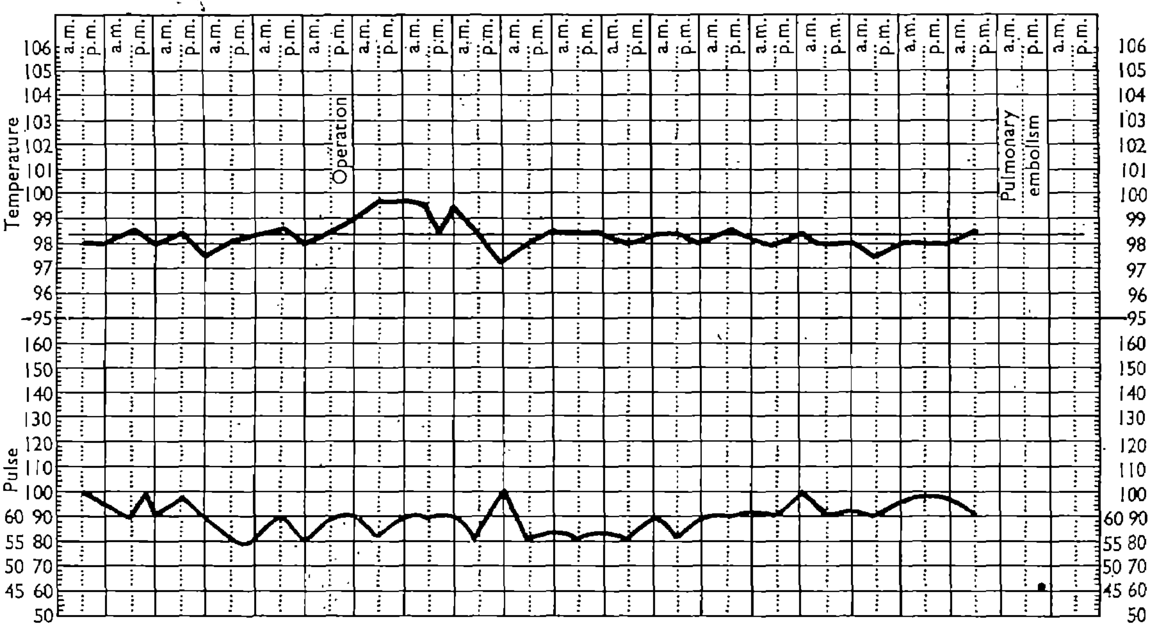


Fig. 3. Normal temperature chart of the 42-year old woman who died from massive pulmonary embolism.

lumen has taken place. This disadvantage seriously limits the value of Doppler ultrasound as a screening technique. ^{125}I-fibrinogen uptake is even less able to detect iliac vein thromboses which are the chief source of major embolism.

Study of the temperature chart has proved of little value. While an unexplained postoperative pyrexia may indicate a deep vein thrombosis requiring further investigation with phlebography, some patients with major thrombosis have no elevation of temperature, and other patients at risk have some septic focus to account for the pyrexia.

The inadequacy of available monitoring techniques emphasizes the importance of establishing simple and reliable methods of prophylaxis.

Acknowledgements

We wish to thank Mr J. M. Pullan and Mr F. B. Cockett for permission to study patients under their care. We also thank Mr T. Brandon of the

Photographic Department of St Thomas's Hospital for the preparation of the illustrations and Mrs E. K. H. Miles for typing the manuscript.

References

EVANS D. S. (1971) The early diagnosis of thrombo-embolism by ultrasound. *Ann. R. Coll. Surg. Engl.* **49**, 225–249.

EVANS D. S. and COCKETT F. B. (1969) Diagnosis of deep-vein thrombosis with an ultrasonic Doppler technique. *Br. Med. J.* **2**, 802–804.

FARIS I. B., ROSENGARTEN D. S. and DUDLEY H. A. F. (1972) Temperature-chart analysis in the diagnosis of postoperative deep-vein thrombosis. *Lancet* **2**, 775–776.

MCILROY R. F. (1972) The routine use of ultrasound for the diagnosis of postoperative deep-vein thrombosis in a district general hospital. *Br. J. Surg.* **59**, 133–135.

SIGEL B., POPKY G. L., WAGNER D. K., BOLAND J. P., MAPP E. MCD. and FEIGL P. (1968) Comparison of clinical and Doppler ultrasound evaluation of confirmed lower extremity disease. *Surgery* **64**, 332–338.

Br. J. Surg. Vol. 62 (1975) 186–188

Surgical management and problems of heart pacing*

J. BORRIE AND I. LICHTER†

SUMMARY

Experience with 40 patients and 150 pacemakers is reviewed. In 13 patients the initial pacing was by epicardial electrodes and in 27 by transvenous catheter electrodes. When epicardial systems were used, two electrodes were always fixed to the heart, the additional electrode being provided for temporary pacing and as a spare in case of future need. The battery unit was usually buried behind the rectus abdominis muscle. Vacuum drainage of the pacemaker pocket was used and was considered helpful in avoiding some complications.

The right cephalic vein was preferred for transvenous pacing but existing venous abnormalities sometimes required use of the external jugular vein. Five patients had epicardial systems changed to transvenous ones, and in 5 the reverse procedure was needed. Pacemaker battery problems included inadequate soft tissue protection for the unit, epoxy resin fracture, titanium case leak and problems relating to design change and the special needs for overseas travel. While the danger from diathermy and radiofrequency is now recognized, similar dangers exist for those paced by 'demand' units in large electromagnetic fields.

BETWEEN 1962 and 1973 cardiac pacing was instituted in 40 patients at Dunedin, and in that time 150 pacemaker units were used. The pacemakers used were at first Elema-Schonander units from Sweden and more recently Telectronics from Australia. On one occasion an Electodyne pacemaker was inserted. This paper reviews that experience with emphasis on the surgical and technical aspects.

Patients

There were 27 males and 13 females. The age distribution is shown in *Table I*.

Table I: AGE DISTRIBUTION OF THE PRESENT SERIES

Age (yr):	No. of patients:
31–40	3
41–50	1
51–60	4
61–70	15
71–80	17
Total	40

Thirty-five of the 40 were paced for heart block, and 5 patients for 'sick sinus syndrome'. In 13 patients the initial pacing was by epicardial electrodes and in 27 by transvenous catheter electrodes.

In 5 patients a change from epicardial to transvenous pacing was later needed; in another 5 there was a change from transvenous to epicardial pacing.

Epicardial pacing

Our first patient had his pacemaker inserted in September 1962 when aged 66 (Borrie and Lichter, 1964). He is still alive and well 13 years and 11 pacemakers later.

Operative approach

The incision for epicardial pacing has usually been a left anterior fifth intercostal space thoracotomy, which gives ready access to the pericardial cavity. Two platinum electrode buttons are sewn on to the myocardium, usually of the right and left ventricles. Two sutures fix the platinum button, and a third steadies the adjacent electrode, so that good contact is maintained. Even when using unipolar pacemakers it has been our policy to insert two platinum electrodes, one for pacing and the other as a spare in case of electrode fracture, or for connecting to a sterile wire from a temporary external unit during pacemaker change.

A trans-sternal incision was used by one of us (J. B.) in a patient who had had a right pneumonectomy 15 years earlier. An attempt at placing a transvenous electrode had failed and it was considered inadvisable to disturb the left lung by a left thoracotomy. The xiphoid and lower sternum were therefore split vertically and access was enhanced by an approach between the xiphisternal origins of the diaphragm, thus enabling the electrodes to be sutured to the inferior surface of the heart.

Pacemaker site

The most favoured site for burying the epicardial pacemaker unit has been in the left rectus sheath, behind the rectus abdominis muscle. A transverse skin incision at umbilical level has proved satisfactory, followed by a vertical rectus sheath incision. If necessary, the incision may be extended into the adjoining rectus muscle sheath to place the pacemaker with its long axis across the midline. However, when using the rectus sheath it is necessary to avoid the lower quarter where only transversalis fascia constitutes its posterior layer. A pacemaker placed in this site later prolapsed into the pelvis.

While it is convenient to fashion a pocket in the axilla, breast or the fat of the ventral abdominal wall, in the long term problems have arisen at these sites so that we now favour the deeper site in the right or left rectus sheath. The electrodes are brought down into the pocket by means of a long metal guide, passed from the pocket to the left pleural cavity. Loops of electrode are left at both the cardiac and pacemaker ends of the system, being coiled outside the pericardium above, and behind the pacemaker below.

---

* This paper was presented at the meeting of the Cardiac Society of Australia and New Zealand in the University of Otago Clinical School at Christchurch in September 1973.

† Department of Surgery, Otago Medical School, and the Southern Regional Thoracic Surgical Unit, Dunedin, New Zealand.

Vacuum drainage

We have found vacuum drainage of the pacemaker pocket an aid to rapid healing. Up to 25 ml of tissue fluid have on occasion drained daily for up to 10 days after operation.

Wound resuture

In 2 patients pacemaker pocket wounds have required early resuture—once when skin sutures were mistakenly removed on the fifth postoperative day, and once on the tenth postoperative day following suture removal in a patient whose wound had been closed without vacuum drainage. Both responded to immediate secondary suture.

Transvenous pacing

Our cardiologists first used temporary catheter pacing electrodes in 1964, and permanent implantable transvenous electrodes in 1967.

Vein catheterization

In catheterizing veins a small disposable plastic vein retractor has proved invaluable, as has a simple binocular loupe that allows normal or magnified vision. The image intensifier is always available. We have found that the Elema-Schonander catheter electrodes require support from a cardiac catheter guide to help easy placement in contact with the right ventricular myocardium.

In earlier patients the right or left external jugular vein was used, placement of the electrode being aided initially by standard screening X-ray equipment, and later by an image intensifier. The electrode was usually placed behind the clavicle using Semb pneumonectomy forceps. Later an appropriately shaped steel hook was designed to facilitate this manœuvre. The electrode was then brought down to the rectus sheath and buried behind the right rectus abdominis muscle.

As the external jugular vein is comparatively superficial, it is not surprising that 3 patients, by constantly scratching their cervical scars, in time caused wound breakdown, wire prolapse and even wire fracture. Thus, although the external jugular vein has been used fourteen times, the cephalic vein is now favoured and has been used thirteen times. It is preferred because it is more deeply placed and disturbance by the patient is less likely. Further, it avoids the step of passing the electrode *behind* the clavicle.

Anatomical variations of both the external jugular and cephalic veins have at times dictated which vein was used.

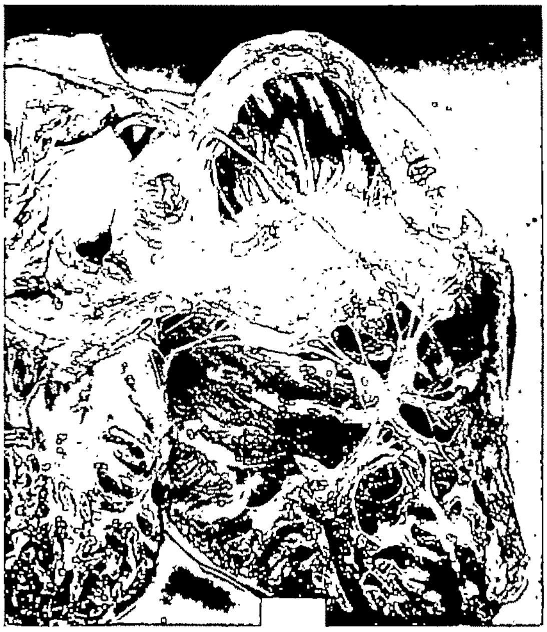


Fig. 1. View of left leaf of the tricuspid valve of a patient who had been successfully paced for 15 months, and who came to autopsy with aortic stenosis. The pacemaker electrode had passed between two chordae tendineae without causing chordal rupture.

Electrode placement problems

In 2 patients who came to autopsy an opportunity was provided for studying the transvenous catheter electrode *in situ*. In both the electrodes were firmly embedded in the right ventricular myocardium. In one the electrode had passed between the chordae tendineae of the tricuspid valve and had been there for 15 months without causing chordal rupture (*Fig.* 1).

Electrode displacement problems

In 5 patients displacement of the catheter electrode into the right atrium occurred, with loss of heart pacing. In one of these the electrode lay near the diaphragm and caused persistent hiccups. In another the electrode slipped from the heart into the liver. The time lapse between implantation of these transvenous electrodes to loss of 'pacing contact' varied from 2 months to 15 months.

Change from transvenous to epicardial pacing

In the 5 patients with persistent displacement of the transvenous electrode a change was made to an epicardial system.

Change from epicardial to transvenous pacing

Five of the 13 epicardial systems were changed to transvenous systems for the following reasons: fractured electrode, 1 patient; sinuses associated with pacemaker, 2 patients; sinuses associated with electrodes, 2 patients. The sinuses occurred usually after more than 5 pacemaker unit changes, and indicate a hazard to be faced where battery life is of the order of just 2 years.

Electrode problems

These have involved:

a. Skin breakdown as a result of scratching the supraclavicular electrodes at the site of entry into the external jugular vein. This problem has not arisen with cephalic vein electrodes.

b. Sinuses at other sites due to 'surfacing' of the electrode on ribs.

c. Lead fractures, either near the pacemaker unit or, if transvenous, near the site of entry into the vein.

Pacemaker unit problems

Trauma to pacemaker pocket

One patient with a right rectus sheath pacemaker connected to a transvenous system for 'sick sinus syndrome' felt so fit postoperatively that, when showing his biceps to his neighbour while lawnmowing, he was struck on the pacemaker by the mower. He did not report the accident but 'poulticed' the unit to 'draw it to the surface'. The result was a haematoma sinus that, despite resiting the unit, did not heal. Because infection later tracked up to his neck producing an abscess at the entry point of the electrode into the right external jugular vein, the system had to be completely removed. Eighteen months after this excision he has had no further attacks of bradycardia, nor has a further unit been inserted.

Patients are advised to protect the pacemaker from body blows and are urged to report early any change in relation to the pacemaker site. Problems encountered have included the development of fluid around the pacemaker and inflammation or erosion of the overlying skin.

'Runaway' pacemakers

On two occasions a pacemaker suddenly increased its rate beyond 200 pulses per minute. This is a surgical emergency demanding immediate removal of the pacemaker. In an early model pacemaker, where there were bursts of 300 pulses per minute, the epoxy resin had fractured, producing a short circuit. In another instance a Telectronic unit developed a leak in the titanium case, producing a short circuit.

Manufacturing problems

'Takeovers' of pacemaker companies have led to inability to match existing implanted systems with the 'new product', and in our experience these unfortunate patients have had to have an entirely new system implanted in a new site.

Overseas travel

It has been possible to send paced university staff on sabbatical leave even to Japan or India—where replacement costs could be high—by having the patient take on loan a sterile unit supplied through the Regional Hospital Board. The patient must take letters signed by the surgeon to cover customs problems. Surgical and cardiological details should be supplied for those who may be consulted abroad.

Radiofrequency, diathermy and pacemakers

In a previous paper we described the hazards of radiofrequency and the use of diathermy which can trigger certain pacemakers into bursts of activity to produce ventricular fibrillation (Lichter et al., 1965). Since our experiments and reports of this hazard it has become Health Department policy both in the United Kingdom and in New Zealand to warn against the use of diathermy in the presence of any cardiac pacemaker.

However, similar dangers still exist in heavy industry using high frequency currents producing large electromagnetic fields, e.g. aluminium smelters, where some 'demand pacemakers' can be adversely affected. Patients should be warned of this, especially if they go sightseeing through heavy industry.

Nuclear-powered pacemakers

We have not yet had occasion to insert a nuclear-powered unit, but can see a very real place for such units, especially in patients whose life expectancy with pacemaker support is more than 10 years, as in a younger patient with 'sick sinus syndrome'. We have noticed that with the present battery units, the more frequent the change, the greater is the risk from infection or delayed healing of the fibrous tissue that inevitably increases with each pacemaker change.

In conclusion, pacemakers have proved life-saving devices for those with heart block, allowing normal activity up to 12 years from the first implanting. Occasionally their management may be punctuated by episodes that demand tedious and exacting attention from cardiologists, surgeons, technicians and theatre staff, and considerable patience and understanding from the patient. Strict care with basic surgical principles reduces these hazards to a minimum.

Acknowledgements

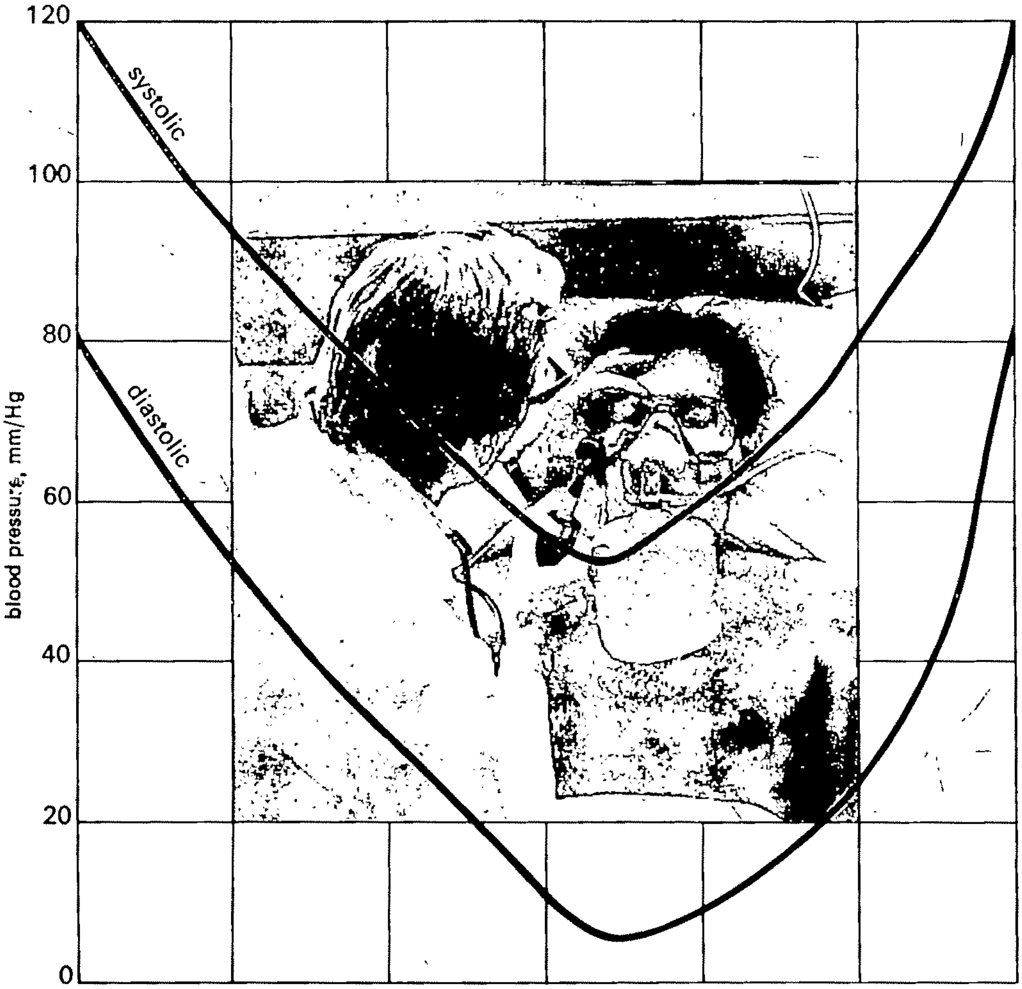
This paper records one facet of teamwork in which the cardiologists involved have been Professor J. D. Hunter, Professor T. V. O'Donnell, Dr Amarassingham and Dr Norma Restieaux. Their help is gratefully acknowledged, as is that of Mr N. Miller, Mr E. Cooper and Mr L. Wong for electronic supervision and Miss N. Richardson for secretarial assistance.

References

BORRIE J. and LICHTER L. (1964) Artificial pacing for heart block; experimental and clinical approach. *NZ Med. J.* **63**, 31–38.

LICHTER I., BORRIE J. and MILLER W. N. (1965). Radiofrequency hazards with cardiac pacemakers. *Br. Med. J.* **1**, 1513–1518.

Survival rate in shock
can be increased with massive
doses of corticosteroids



Injection DECADRON® Shock-Pak

Dexamethasone sodium phosphate/MSD

20 mg/ml (new strength)

In severe shock, treatment with Injection 'Decadron' Shock-Pak is an adjunct to, and not a substitute for, specific or supportive measures that the patient may require, e.g. restoration of circulating blood volume, correction of fluid and electrolyte balance, oxygen, surgical measures, and antibiotics.

Supplied in 5 ml ampoules containing per ml, dexamethasone sodium phosphate equivalent to 20 mg dexamethasone. Detailed information is available to physicians on request. ® denotes registered trademark.

MSD Merck Sharp & Dohme Limited
Hoddesdon, Hertfordshire. Telephone Hoddesdon 67123

3-2820 (IMC)

Br. J. Surg. Vol. 62 (1975) 189–200

Postoperative problems and management after hepatic resection for blunt injury to the liver

T. VAJRABUKKA, A. L. BLOOM, M. SUSSMAN, C. B. WOOD AND L. H. BLUMGART*

SUMMARY

The postoperative problems and management of 8 patients following right hepatic lobectomy for blunt liver injury are discussed. Multiple injury and in particular chest injury are of importance. Respiratory distress may be insidious in onset and must be anticipated. Most patients require at least temporary positive pressure ventilation.

Liver regeneration is rapid and histological evidence of regenerative hyperplasia is present within 3 days of injury.

Hypoglycaemia of a degree sufficient to threaten life may occur postoperatively, particularly in the first 48 hours. Jaundice may be a worrying postoperative feature, but the use of T-tube drainage after hepatic lobectomy will enable any possible extrahepatic obstruction to be excluded. Hypoproteinaemia and hypo-albuminaemia occur in the immediate postoperative period, and recovery rapidly follows the peak period of regenerative activity of the liver. Normal levels are regained by the fourth to sixth postoperative weeks.

Prophylactic antibiotics have no place in the postoperative management of blunt liver injury.

Haemorrhagic diathesis is common after hepatic resection and is of a complex nature. Intravascular coagulation may occur and factor V deficiency is common. The mainstay of treatment is transfusion of fresh blood.

THE mortality for blunt liver injuries has decreased from 60 per cent (Mikesky et al., 1956; Foster et al., 1968) to 30 per cent or less (Little and Williams, 1969; Walt, 1969; Blumgart and Vajrabukka, 1972; Donovan et al., 1973). The improvement has been the result of better techniques of resuscitation, adequate blood transfusion and improved management of the more extensive injuries. Several authors have drawn attention to the danger of gauze packing for large destructive wounds of the liver (Crosthwait et al., 1962; Hanna et al., 1965; McClelland and Shires, 1965), and hepatic resection has been accepted in the management of very extensive blunt liver injuries (Walt, 1969; Balasegaram, 1970; Little, 1971; Blumgart and Vajrabukka, 1972). This more agressive surgical approach with resection of large segments of damaged tissue has been based on an appreciation of the extraordinary regenerative capacity of the liver (Weinbren, 1959; McDermott et al., 1963; McDermott, 1970; Blumgart et al., 1971).

The postoperative period following major hepatic resection can be complicated by metabolic disturbances which, if not anticipated and recognized, can be life-threatening (Pack and Molander, 1960; McDermott et al., 1963; Almersjö et al., 1969; Aronsen et al., 1969). These metabolic disturbances, together with problems arising as a direct result of multiple injury, massive blood transfusion and infection, form a complex clinical problem.

This paper reports experience of the postoperative management and problems encountered following right hepatic lobectomy for blunt liver injury carried out in 8 previously healthy patients.

Patients

The essential features of the 8 cases are summarized in *Table I.* All sustained their injuries as a result of road traffic accidents. Two were injured in crushing accidents, 1 pedestrian was hit by a passing car, 1 fell from the back of a moving milk van and the other 3 were the drivers of either a motor-cycle or a car. All were young (aged between 9 and 39 years) and all had been in previously good health.

Five cases were operated on within 3 hours of injury although in one of these cases (*Case* 1) a first operation entailed simple suturing of the liver, and right hepatic lobectomy had to be carried out for recurrent haemorrhage 10 hours later. This patient has been previously reported (Taylor and Blumgart, 1971). In the remaining 3 cases there was a longer delay between the time of injury and the time of operation. One patient (*Case* 4) was operated on 12 hours after admission, the definitive signs of intra-abdominal haemorrhage being absent until this time. One patient was not operated on until the sixth hour after injury as a result of delay in transport to hospital. The remaining patient was admitted to another hospital with multiple injuries and was transferred to our care 72 hours after the accident, deeply jaundiced, anuric and with obvious signs of peritoneal irritation (*Case* 6).

In each instance the hepatic injury was extensive and, apart from minor lacerations to the left lobe, was confined to the right lobe of the liver. The parenchymal destruction in each case (*Fig.* 1) could not be dealt with adequately by any other means than formal hepatic resection, the indications for which

---

* University Department of Surgery, Glasgow Royal Infirmary, and Departments of Haematology and Medical Microbiology, Welsh National School of Medicine, Cardiff.

Present address of T. Vajrabukka: Chulalongkorn University Medical School, Bangkok, Thailand.

Requests for reprints to Professor L. H. Blumgart, University Department of Surgery, The Royal Infirmary, Glasgow.

Table I: DETAILS OF THE PRESENT SERIES

Case	Sex	Age	Causes	Associated injury	Time from accident to operation	Units of blood transfused	Postoperative complications	Weight of liver resected (g)	Remarks
1. J. F.*	M	21	Crushed by a lorry	Flail chest, bilateral pneumo-haemothoraces, concussion	3 h+second operation 10 h after first	18	Respiratory difficulty, tracheostomy and PPV, pneumonia, empyema, wound infection, haemorrhagic diathesis, early hypoglycaemia (mild), terminal renal shutdown	Not recorded	Died 10 days after operation. Post-mortem showed extensive lung contusion, bronchopneumonia, oedematous pancreas with necrotic foci
2. M. R.	M	22	Motor cyclist in collision with a tree	Concussion, fracture of right forearm	3 h	20	Respiratory difficulty, tracheostomy and PPV, haemorrhagic diathesis, pneumonia, infected T-tube bile, subphrenic abscess	650	Survived
3. S.O.*	F	9	Pedestrian hit by a car	Concussion, ruptured spleen	2 h	12	Severe hypoglycaemia, haemorrhagic diathesis, pneumonia, biliary leakage around the choledochotomy site, wound infection, subphrenic abscess	375	Survived
4. S. D.*	M	13	Fell off a milk van	Nil	12 h	4	Transient respiratory difficulty, intermittent hypoglycaemic episodes during subsequent 2 weeks (mild), pneumonia, T-tube bile infection, septicaemia, peritonitis	449	Survived
5. D.O.*	M	23	Crushed by a bus	Multiple long bone and pelvic fractures, ruptured right diaphragm, tear of second part of duodenum, compression necrosis of ascending colon	3 h	22	Haemorrhagic diathesis, right haemothorax	745	Died 10 hours after operation. Post-mortem showed, tear in azygos vein, haemorrhagic necrosis of both adrenals, bronchopneumonia
6. J. M.	M	28	Hit by a car (transferred from another hospital)	Fractures of right tibia, fibula and forearm, ruptured right kidney, concussion	72 h	30	Respiratory difficulty, tracheostomy and PPV, acute renal failure, infected T-tube bile, septicaemia, haemorrhagic diathesis, intermittent hypoglycaemic episodes during the next 3 weeks (mild), acute pancreatitis, pneumonia, empyema, wound infection	1045	Died
7. R. B.	M	19	Car in collision	Fractures of right humerus, contusion of right lung, laceration of right thigh	2 h	24	Transient respiratory difficulty, pneumonia, wound infection, subphrenic abscess	970	Survived
8. M. D.	F	39	Car in collision	Fractured ribs, cervical vertebral body C5 and pelvic rami, lung contusion, concussion	4–5 h	19	Transient respiratory difficulty, haemorrhagic diathesis	800	Survived

* Included in previous reports (Taylor and Blumgart, 1971; Blumgart and Vajrabukka, 1972).
PPV, Positive pressure ventilation.

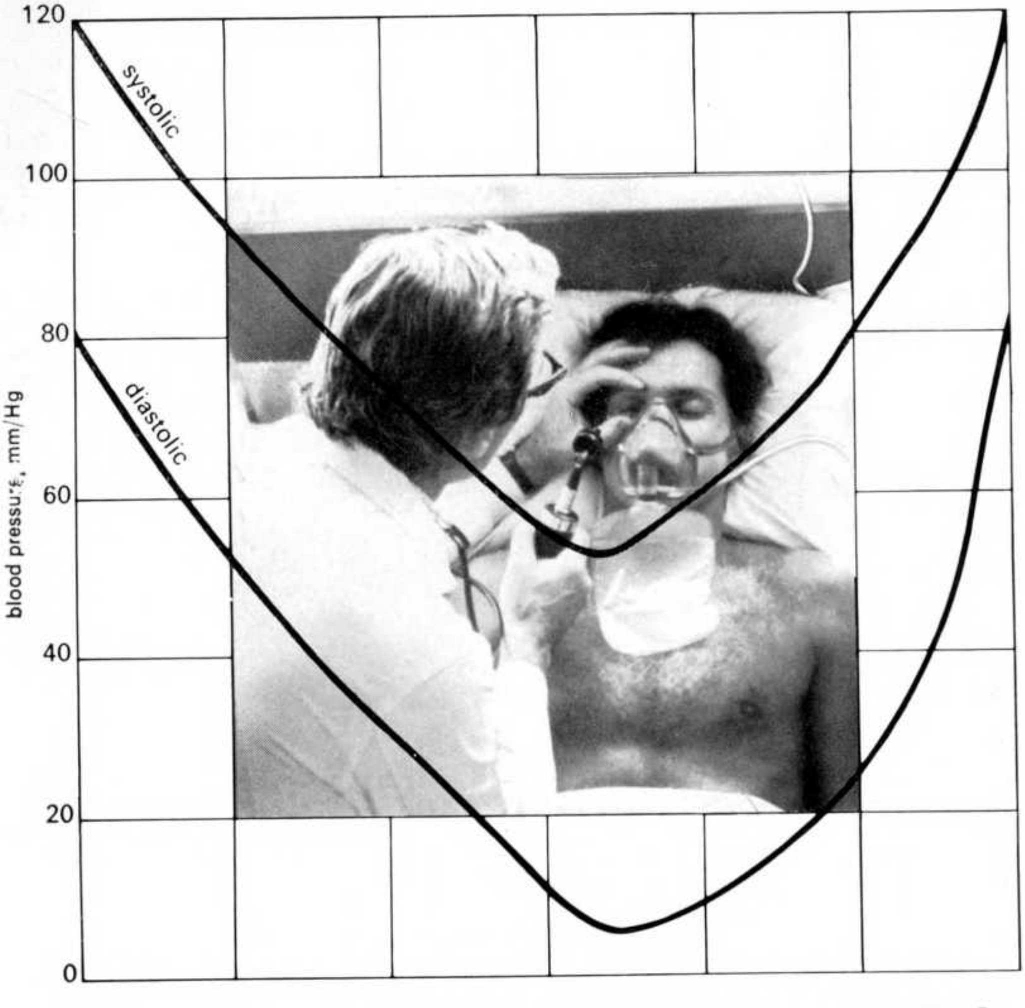
Now paediatrics gets the Seward treatment.

At Seward, we believe that instruments for paediatric surgery are every bit as important as adult instruments.

That's why we spent a long time developing and perfecting our own paediatric range – and we're grateful for the co-operation of so many children's hospitals, paediatric departments and consultants.

Now the range is complete – 580 fine quality stainless steel instruments. Including many which have never before been modified for paediatric use. And some entirely new instruments developed in the Seward workshop.

Survival rate in shock can be increased with massive doses of corticosteroids



Injection DECADRON® Shock-Pak

Dexamethasone sodium phosphate/MSD

20 mg/ml (new strength)

In severe shock, treatment with Injection 'Decadron' Shock-Pak is an adjunct to, and not a substitute for, specific or supportive measures that the patient may require, e.g. restoration of circulating blood volume, correction of fluid and electrolyte balance, oxygen, surgical measures, and antibiotics.

Supplied in 5 ml ampoules containing per ml, dexamethasone sodium phosphate equivalent to 20 mg dexamethasone. Detailed information is available to physicians on request. ® denotes registered trademark.

MSD Merck Sharp & Dohme Limited
Hoddesdon, Hertfordshire. Telephone Hoddesdon 67123

2-2920 (IMC)

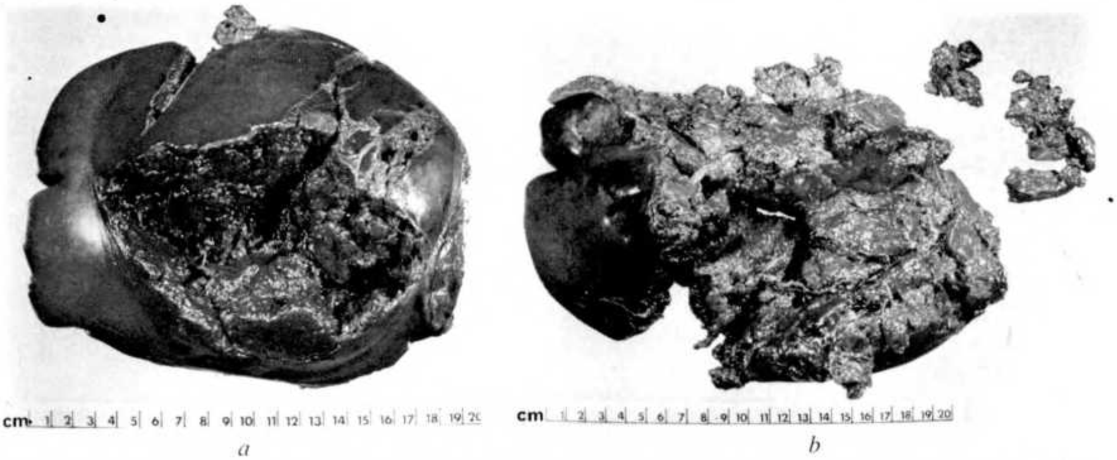


Fig. 1. Resection specimen showing the extent of liver parenchymal destruction to the right lobe of the liver necessitating right hepatic lobectomy. *a*, The dome of the right lobe. *b*, The cut surface of the right lobe, demonstrating the explosive destruction of liver tissue.

have been previously described (Blumgart and Vajrabukka, 1972; Blumgart, 1973). All 8 patients underwent right hepatic lobectomy via a right thoraco-abdominal incision, the technique employed being essentially that described by Quattlebaum and Quattlebaum (1959) and by Lloyd-Davies and Angell (1957). All were managed with postoperative chest drains, drainage to the right subhepatic space and T-tube drainage as suggested by Merendino et al. (1963).

Postoperative management

The patients were returned to the ward and the need for blood transfusion was monitored according to the blood pressure, pulse rate and central venous pressure recordings. An intravenous infusion of 1 litre of normal saline and 2 litres of 5 per cent dextrose saline solution for 24 hours formed the basis of intravenous therapy. Oral fluids were prescribed in the early postoperative period and the nasogastric tube was aspirated hourly. The volume of drainage from the chest drain, the subdiaphragmatic drain(s) and the T-tube was monitored, as was the urinary output.

All except one patient had superficial flesh wounds and in addition to wound débridement each received a booster dose of tetanus toxoid. All but one of the patients received an intramuscular course of ampicillin 250 mg 6-hourly. Vitamin K was administered in a dose of 10–20 mg intramuscularly daily.

Frequent estimations were made of the haemoglobin, packed cell volume, blood glucose, serum amylase and serum electrolytes. Liver function was assessed daily by recording changes in the serum proteins, serum bilirubin, alkaline phosphatase and serum transaminases.

Regular estimations were made of the blood gases and the acid-base status of the patients. Endotracheal intubation, tracheostomy and positive pressure ventilation (PPV) were used when indicated.

Table II: ASSOCIATED VISCERAL INJURY

Organ:	Frequency:
Spleen	1
Kidney	1
Duodenum	1
Ascending colon	1
Diaphragm	1
Azygos vein	1
Lungs	3*

* One was bilateral.

A full haematological survey for clotting factors was undertaken in all the patients, and if possible, this was done before transfusion was commenced. The haematological studies were repeated daily for as long as necessary.

Samples for bacteriological examination were taken daily from the sputum, tracheostomy site and from all the drainage tubes; other sites were sampled if this was thought necessary.

Postoperative problems and complications

The postoperative problems encountered can be conveniently reported and discussed under four main headings.

1. *Problems arising as a result of multiple injury*

Patients with liver injury seldom have rupture of the liver as an isolated lesion. In a series of 20 cases previously reported by us (Blumgart and Vajrabukka, 1972) the liver alone was injured in only 2.

Of the 8 patients in this report, only one had injury to the liver alone. The others had damage to one or more organs (*Table II*). The frequency of injury to other abdominal organs, particularly in the upper abdomen, makes careful exploration mandatory. The spleen should be examined in all cases, and indeed was found to be ruptured in one of our patients. Injuries to the duodenum and pancreas may easily be missed at laparotomy and must be sought deliberately.

It is of interest that concussion was common and occurred in 5 cases. In 2 (*Cases* 2 and 3) the period of unconsciousness lasted longer than 2 hours with some degree of post-traumatic amnesia after recovery. There were no associated skull fractures in any case.

Musculoskeletal injuries were common (*Table I*), and it is of particular interest that 4 patients had associated fractures of the right upper arm or of the ribs on the right side, and in 1 patient there was an extension 'whip-lash' fracture of the body of C5. The management of these musculoskeletal injuries took second place to the treatment of the liver injuries in our patients. Fractures were temporarily splinted and reduction immobilization carried out at the end of the abdominal operation. Lengthy orthopaedic manipulations were not undertaken and plaster casts were applied in such a way as not to interfere with the process of monitoring the patient's vital signs. Definitive orthopaedic treatment, if required, was carried out electively at a later date. It is of interest that the pattern of skeletal injury, both to the upper limb on the right and to the ribs on the right side, suggested direct trauma to the posterolateral margin of the chest wall as the mechanism of hepatic injury.

The most serious postoperative problem encountered as a result of multiple injury involved damage to the chest. Early postoperative respiratory difficulty was common. Although this was anticipated in 3 cases (*Cases* 1, 7 and 8) with severe injuries, altogether 7 of the 8 patients required endotracheal intubation and positive pressure ventilation. Even such methods were insufficient and in 3 patients tracheostomy proved necessary. It is clearly evident that it was not only the effects of mechanical disruption of the chest alone (e.g. flail chest, pneumothorax) which were life-threatening but also the more subtle complications of blood and sputum retention. Although none of our patients had direct injury to the heart or thoracic aorta, these possibilities must be borne in mind. The signs of traumatic rupture of the thoracic aorta in particular may not be seen until many days after initial injury. A high index of suspicion, repeated examination of the patient and repeated good quality chest X-ray films, including aortography in cases of real doubt, will identify many of these patients in time for definitive treatment.

2. *Problems of postoperative infection*

Infective complications are an ever present danger after hepatic resection. Though many surgeons recommend the prophylactic administration of antibiotics after liver resection (Walt, 1969; Donovan et al., 1973) this practice requires re-examination.

It is clear from our data that infective complications were common despite the use of prophylactic antibiotics. Indeed, the only case (*Case* 8) who did not develop a serious clinical infection (other than a urinary tract infection) was the only patient who did not have antibiotic prophylaxis.

Apart from bronchopneumonia diagnosed at autopsy in 3 cases, there were infections at 22 separate sites in this series of patients (*Table III*). The initial infections were commonly due to single organisms (72 per cent) and the rest (28 per cent) due to at least two organisms. *Escherichia coli* was the most common organism isolated and was involved in over half (56 per cent) of the infected sites. In particular, *E. coli* was found in relation to drains and catheters. In only 2 cases were the first organisms isolated sensitive to the prophylactic antibiotics, but the flora rapidly changed and resistant organisms appeared. In addition, many organisms appeared at the sites where originally only one had been involved. Many of these were highly resistant to antibiotics. Five patients acquired *Candida albicans* infection and in 4 of these more than one site was involved, but in no case was specific therapy required. In 5 patients with infection at more than one site the same organism or organisms were responsible for the infection. This fact, together with the staggered appearance of infection, suggests that the infection spreads from one site to another, and this has obvious implications for nursing procedures.

A positive blood culture was obtained in both patients from whom specimens were taken in the early postoperative period. Infection of T-tube bile was always accompanied by other infection. In one case a subphrenic abscess developed and in another a patient developed localized peritoneal irritation following removal of the T-tube. In one of these patients the infection spread to a pleural effusion.

3. *Haemorrhagic diathesis*

Haemorrhagic diathesis is a well-recognized problem after hepatic resection (Nilehn et al., 1967; Aronsen et al., 1969; Walt, 1969; Little, 1971; Taylor and Blumgart, 1971; Blumgart and Vajrabukka, 1972). For this reason blood coagulation surveys were carried out, if possible on admission, and before transfusion was commenced. The studies were repeated as frequently as necessary.

Method: Platelet counts, prothrombin times, kaolin cephalin times, thrombin clotting times, fibrinogen titres and tests for fibrinolysis were always performed immediately after venepuncture. Coagulation factor assays were usually performed soon after venepuncture but occasionally on samples of plasma stored at −30°C for a maximum of 3 days.

Platelet counts were performed on a Coulter Model F electronic counter, prothrombin times and thrombin clotting times were performed as described by Biggs and Macfarlane (1962) and kaolin cephalin clotting times by the method of Proctor and Rappaport (1961). Fibrinogen titres were measured by the method of Sharp et al. (1958). Using this method the normal fibrinogen level was 1/32 to 1/128 which is approximately equivalent to 200–500 mg/100 ml (Giddings and Bloom, 1971). Fibrinogen levels below 100 mg/100 ml were indicated by a titre below 1/16. Clottable fibrinogen was measured by the method described by Varley (1967). Increased fibrinolysis was demonstrated by a dilute clot lysis method (Giddings and Bloom, 1971). Fibrin degradation products (FDP) were measured by the Wellcome Laboratories modifications of the method of Merskey et al. (1966). Factor VIII assays were performed by the method of

Table III: DETAILS OF INFECTIVE COMPLICATIONS

Complication	Case no. 1	2	3	4	5	6	7	8
Infected sputum	+	+		+		+	+	
Bronchopneumonia								
Clinical	+	+	+	+		+	+	
Necropsy	+				+	+		
Empyema	+					+		
Surgical wound infection	+		+			+	+	
Infection of T-tube bile		+		+		+		
Subphrenic abscess		+	+				+	
Peritonitis				+				
Septicaemia (early)				+		+		
Urinary tract infection	+		+			+		+
Prophylactic antibiotics given	+	+	+	+	+	+	+	—
Sensitivity of organism to prophylactic antibiotic	—	—	—	—		—	—	NR
Outcome	Died at 10 d	Survived	Survived	Survived	Died at 10 h	Died at 20 d	Survived	Survived

NR, Not relevant.

Table IV: RESULTS OF COAGULATION FACTOR TESTS ON DAY WHEN THEY WERE MOST ABNORMAL

Case	Day	Platelets (×10³/mm³, 150–400*)	PT (s)	KCCT (s)	TCT (s)	Fibrinogen titre (1/32–1/128*)	Plasma fibrinolysis (Neg.*)	FDP (μg/ml, 12*)	Factor (%, 50–150*) V	VII+X	VIII	IX	X
2	1	28	22 (11)	68 (36)	60 (11)	1/4	Neg.	—	—	—	—	—	—
3	2	165	24 (14)†	59 (44)	14 (12)	1/32	Pos.	160	—	—	—	87	—
4	2	108	26 (14)	55 (41)	12 (11)	1/128	Neg.	—	—	—	—	—	—
5	1 (a.m.)	10	23 (14)	65 (39)	14 (11)	1/64	Neg.	—	8	—	32	25	48
	1 (p.m.)	127‡	20 (13)	61 (44)	17 (10)	1/32	Neg.	—	6	—	32	17	—
6	2	55	15 (13)	34 (35)	12 (12)	1/64	Neg.	50	—	—	—	—	—
	20§	33	17 (12)	55 (40)	23 (14)	1/128	Neg.	320	—	—	—	—	—
7	1	108	16 (13)	31 (30)	14 (13)	1/64	Neg.	20	19	86	71	58	38
	8	161	16 (14)	37 (39)	11 (12)	1/128	Neg.	—	270	150	190	104	180
8	1	89	18 (13)	31 (31)	12 (11)	1/128	Neg.	10	10	44	105	66	27

PT, Prothrombin time. KCCT, Kaolin cephalin clotting time. TCT, Thrombin clotting time. FDP, Fibrin degradation products. Control values in parentheses.

* Normal range.

† Corrected by normal serum, not by adsorbed plasma.

‡ Serum amylase 2000 units.

§ Platelet transfusion given.

Poll and Robinson (1959), factor V assays by the method of Speer and Borges (1962), factor IX assays as described by Hardisty and Ingram (1965) and factor II assays by the two-stage procedure (Biggs and Macfarlane, 1962). Factor X assay and an assay sensitive to deficiency of either factor VII or X were performed by the method of Denson (1961) using Russel viper venom–cephalin mixture for the former assay and saline extract of brain for the latter.

Results: Coagulation defects occurred in all the patients and were sometimes of a complex nature. The results obtained on the days when the coagulation defects were most marked are summarized in *Table IV*. The causes of the coagulation defects may be multiple and those which may have been responsible in our patients are shown in *Table V*. In only 2 cases could the cause be confidently established. One of these cases (*Case 2*) showed classic features of the defibrination syndrome with a preoperative low platelet count, low fibrinogen level and prolonged prothrombin time, thrombin time and kaolin cephalin clotting time (*Table VI*). This patient received 20 units of blood

Table V: HAEMOSTATIC DISORDERS: PROBABLE CAUSES

Case no.	Probable aetiological factors (order of importance)
2	Intravascular coagulation
3	Liver impairment
4	Liver impairment, transfusion
5	Intravascular coagulation, liver impairment
6	Intravascular coagulation, transfusion
7	Intravascular coagulation, liver impairment
8	Liver impairment, transfusion

Table VI: TESTS OF HAEMOSTASIS IN CASE 2

Day	Platelets (×10³/mm³)	PT (s)	KCCT (s)	TCT* (s)	Fibrinogen titre
1 (preop)	28	22 (11)	68 (36)	60 (11)	1/4
1 (postop)	153	13 (12)	42 (44)	11 (11)	1/32
2	150	13 (12)	43 (42)	9 (9)	1/32
3	80	15 (12)	43 (44)	10 (10)	1/128
4	89	13 (12)	44 (43)	8 (8)	1/32
5	144	13 (12)	42 (42)	13 (13)	1/32

See Table IV for key to abbreviations. Control values in parentheses.

Table VII: TESTS OF HAEMOSTASIS IN CASE 3

Day	Platelets (×10/^{3}mm^3)	PT (s)	KCCT (s)	TCT (s)	Fibrinogen titre	FDP (μg/ml)	Plasma fibrinolysis	Factor (%) II	V	VIII	IX	X	VII+X
1	105	18 (14)	65 (47)	15 (11)	1/32†	—	Neg.	46	70	40	40	45	90
2	165	24 (14)*	59 (44)	14 (12)	1/32‡	160	Pos.	—	—	—	87	—	—
3	145	17 (13)	35 (42)	11 (11)	1/64	—	Neg.	—	—	—	—	—	—
4	—	14 (12)	35 (37)	—	—	—	—	—	—	—	—	—	—

See Table IV for key to abbreviations. Control values in parentheses.
* Corrected by normal serum. Not corrected by normal adsorbed plasma.
† 219 mg/100 ml.
‡ 1/128 in epsilon aminocaproic acid.

Table VIII: TESTS OF HAEMOSTASIS IN CASE 6

Day	Platelets (×10^3/mm^3)	PT (s)	KCCT (s)	TCT (s)	Fibrinogen titre	FDP (μg/ml)	Thrombotest (%)
1 (11.30 p.m., intra-op.)	170	14 (13)	34 (37)	13 (13)	1/128	6·3	56
2 (10.00 a.m.)	75	15 (14)	35 (37)	15 (13)	1/64	50	—
2 (4.00 p.m.)	55	15 (13)	34 (35)	12 (12)	1/64	—	—
3	104	16 (15)	34 (35)	17 (13)	1/64	202	—
4	83	—	—	240+(13)*	1/64	101	—
6	94	15 (13)	31 (36)	11 (12)	1/64	—	—
11	124	15 (14)	40 (38)	15 (12)	1/64	—	—
12	120	15 (14)	40 (38)	15 (12)	1/64	—	—
18	59	14 (13)	40 (36)	19 (12)	1/128	—	—
20	33	17 (12)	55 (40)	23 (14)	1/128	320	—

See Table IV for key to abbreviations. Control values in parentheses.
* Heparinized for haemodialysis.

before and during surgery, 10 of which were fresh blood. The abnormalities were shown to be rapidly corrected following evacuation of the haematoma, surgical repair and transfusion of fresh blood. There was transient mild thrombocytopenia on the third and fourth postoperative days, the cause of which was not determined but could have been due to loss of transfused platelets.

In another case (*Case* 3) liver impairment alone could account for most of the abnormalities found (*Table VII*). This patient received 9 units of stored blood during surgery and 3 units of fresh blood during the next 24 hours. The studies showed only minor deficiencies of platelets and coagulation factors. On the day following surgery the main defects were prolonged prothrombin times, which were corrected by addition of normal serum, and increased fibrinolysis consistent with hepatic impairment. The raised FDP could have been the effect of the increased fibrinolytic activity or due to absorption from the haematoma and there was no firm evidence of intravascular coagulation.

The findings in the other 5 cases were not amenable to such simple explanations and it is probable that they resulted from several causes (*Table V*). The presence of thrombocytopenia of greater or lesser degree, deficiency of factor V and sometimes prolonged thrombin times or raised levels of FDP suggested some degree of intravascular coagulation, but this was by no means certain in every case.

The low levels of factor V were particularly striking and would be consistent with impaired liver synthesis. Indeed, we have since noted similar deficiencies of factor V following extended right hepatic lobectomy for carcinoma of the liver. In one case (*Case* 6) intravascular coagulation (*Table VIII*) occurred as a terminal event in association with acute pancreatitis. This patient had received 10 units of stored blood soon after injury and 20 units (4 fresh) during operation. The coagulation studies obtained during and immediately after hepatectomy were all within the normal range. Postoperatively there was a fall in the platelet count and a rise of FDP. This could have been due to intravascular coagulation but may have been the result of transfusion and the absorption of FDP from haematoma. On the other hand, terminally there was a profound fall in the platelet count with a prolonged thrombin clotting time, abnormal prothrombin and kaolin cephalin times and raised FDP. These changes were associated with marked elevation of the serum amylase (2000 Somogyi units) and were consistent with intravascular coagulation complicating pancreatitis.

The common occurrence of thrombocytopenia, possibly due to transfusion or intravascular coagulation, and the low levels of factor V, probably the result of defective liver production, were particularly noteworthy.

4. *Liver regeneration and associated metabolic problems*

The liver exhibits a remarkable regenerative capacity after major resection. In man this regenerative activity commences soon after operation and progresses

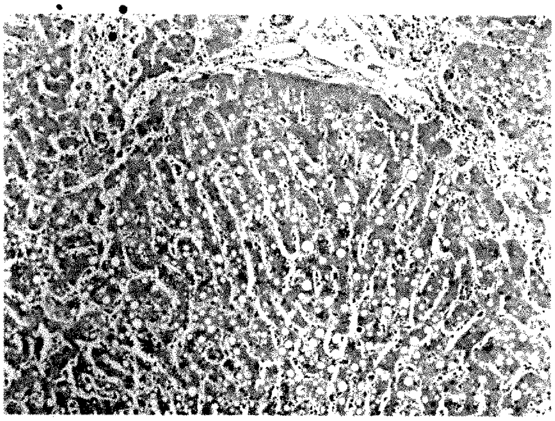


Fig. 2. Photomicrograph of regenerating liver at 24 hours after partial hepatectomy showing double cell plates. Note the larger hepatocytes in relation to portal tracts as compared with those in a more central site within the lobule. (× 60.)

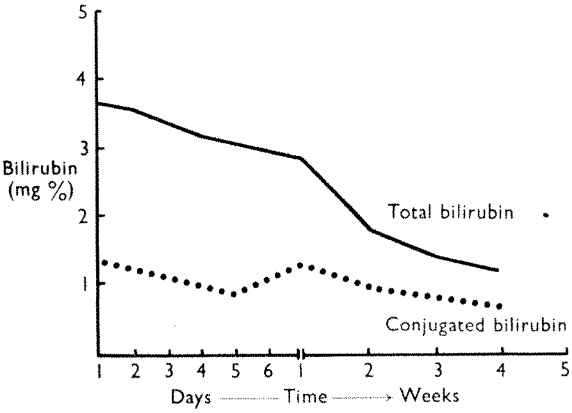


Fig. 4. *Case* 7. Rise in serum bilirubin level after hepatic resection with the conjugated fraction as the main component (type II).

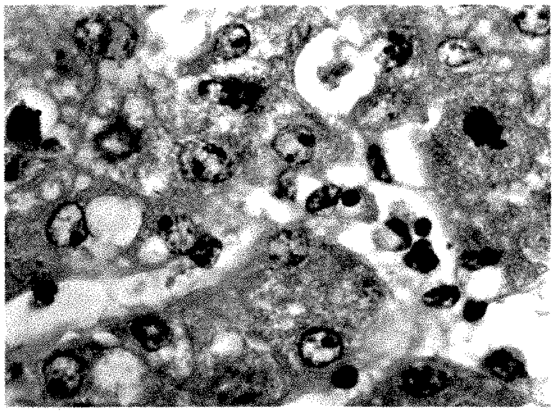


Fig. 3. Photomicrograph of regenerating liver after partial hepatectomy showing increased mitotic activity. (× 600.)

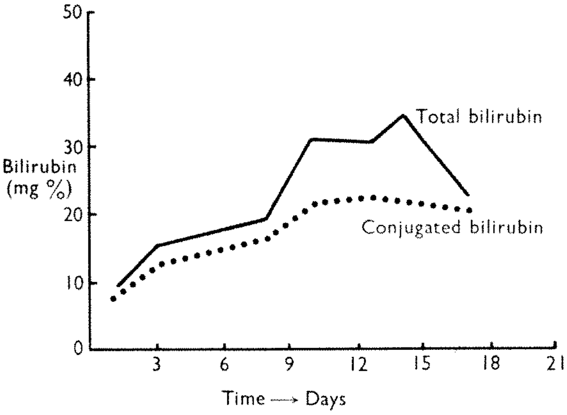


Fig. 5. *Case* 6. Rise in serum bilirubin level after hepatic resection with the unconjugated fraction as the main component (type I).

rapidly during the early postoperative period. In one of our patients (*Case* 6) who came to operation 3 days after injury the weight of the right lobe of liver resected was 1045 g, and it was also noted that the left lobe of the liver was enlarged. This increase in size was accompanied by histological characteristics of regeneration, double cell plates (*Fig.* 2), and multiple mitotic figures (*Fig.* 3) being clearly visible at this early stage.

Metabolic changes frequently occur following removal of large quantities of liver tissue and are related to the process of liver regeneration.

Serum proteins: The serum albumin level began to fall within 24 hours of hepatic resection. Some recovery was noted between the second and fourth weeks and normal values were attained by the fifth to sixth postoperative weeks (*Table IX*).

Many clinicians recommend intravenous albumin supplements during this period (Pack et al., 1962; McDermott et al., 1963; Aronsen et al., 1969; Balasegaram, 1970), but in spite of intravenous albumin supplements of 75 g daily for 5 days in 2 cases (*Cases* 1 and 2) there was no improvement in the patients' serum albumin levels. We subsequently abandoned the practice of routine albumin supplements, with no adverse effects. The total serum protein levels were found to be low on the first postoperative day in all cases, but returned to normal levels within 2–3 weeks despite a persistently low serum albumin fraction. This could account for the lack of any clinical evidence of hypoproteinaemia (e.g. oedema).

Hypoglycaemia: Episodes of hypoglycaemia occurred in 5 of our 8 patients, and in a sixth (*Case* 7) an episode of collapse was treated successfully by the administration of 50 ml 50 per cent dextrose, although objective evidence of hypoglycaemia was not obtained. Blood sugar levels of less than 90 mg/100 ml were regularly recorded in these patients for up to 16 days after injury, but the reduced levels were slight and clinical signs of hypoglycaemia were not always evident. All these episodes occurred despite infusion of 5 per cent dextrose solution. Three of the episodes of hypoglycaemia occurring within the first 48 postoperative

Table IX: SERUM PROTEIN AND SERUM ALBUMIN LEVELS AFTER HEPATIC RESECTION

	Time postop.	Case					
		2	3	4	6	7	8
Total protein (g/100 ml) Normal: 6·8–8·0 g/100 ml	24 h	5·2	5·2	5·6	6·0	6·4	5·4
	1 wk	4·9	5·8	6·2	6·0	6·5	4·6
	2 wk	6·5	6·1	7·4	5·4	6·8	6·8
	3 wk	5·8	5·5	8·3	Patient died	6·6	6·5
	1–2 mth	6·8	7·3	7·2		8·4	8·0
Albumin (g/100 ml) Normal: 3·5–4·8 g/100 ml	24 h	3·3	3·2	4·7	3·1	3·7	3·3
	1 wk	2·8	3·2	3·1	2·5	2·9	2·3
	2 wk	3·0	2·8	3·0	2·2	2·5	2·7
	3 wk	2·6	2·4	3·6	Patient died	2·3	2·8
	1–2 mth	3·4	4·3	4·4		4·4	3·5

Table X: SERUM ALKALINE PHOSPHATASE AND SGPT LEVELS AFTER HEPATIC RESECTION

	Time postop.	Case						
		1	2	3	4	6	7	8
Serum alkaline phosphatase (i.u./l) Normal: 10–40 i.u./l	24 h	140	37	64	45	50	38	28
	1 wk	—	46	68	56	88	39	33
	2 wk	—	56	80	54	70	38	78
	3 wk	—	45	86	107	—	50	78
	1–2 mth	—	45	77	86	—	125	56
SGPT (u./ml) Normal: 5–28 u./ml	24 h	—	330	335	420	232	208	360
	1 wk	—	95	41	65	290	21	80
	2 wk	—	49	8	75	55	15	47
	3 wk	—	16	7	15	—	7	44
	1–2 mth	—	19	7	11	—	13	11

hours were significant in that they produced sweating, tachycardia and collapse.

Jaundice: Jaundice occurred in all our patients and on occasions was a worrying clinical feature. Two patterns emerged from the study of our cases, one in the patients who survived and the other in those who died.

In the patients who survived the rise in serum bilirubin was not great. Indeed, it was no higher than 10 mg/100 ml and reached a peak within the first postoperative week, falling to normal levels by the end of the second week (except for one case in which it remained elevated for 4–5 weeks). In some of these patients the conjugated and unconjugated fractions of bilirubin were measured. It was found that elevation occurred in both fractions but the unconjugated bilirubin fraction showed the greatest rise (*Fig.* 4).

Of the patients who died, one (*Case* 5) died too soon after operation for any detailed biochemical or haematological analysis to be performed, and in one further patient (*Case* 1) the available results were incomplete. Nevertheless, 2 of the cases (*Cases* 1 and 6) had similar features. Both had suffered prolonged hypotensive periods following injury, both had severe postoperative sepsis and both developed renal failure. At necropsy both showed evidence of acute pancreatitis which was severe in *Case* 6. In both these patients the jaundice was severe and very high serum bilirubin levels were reached prior to death (*Fig.* 5). Early rises in serum alkaline phosphatase were noted in both patients at the end of the first week. In contrast to the cases which survived, the serum bilirubin in these cases was mainly of the conjugated variety.

Serum enzymes: Changes in the serum enzymes occurred after resection. A rise in the serum alkaline phosphatase levels occurred during the third and fourth weeks in 3 patients (*Cases* 2, 4 and 8; *Table X*). However, in the patients who died (*Cases* 1 and 6) the rise in serum alkaline phosphatase (*Table X*) occurred somewhat earlier than in the other patients. The serum glutamic pyruvate transminase (SGPT) rose immediately after operation in each instance and then usually fell to normal levels by the second week (*Table X*). Liberation of the enzyme from the damaged liver cells is a likely reason for such rises in the enzyme levels. It is noteworthy that in one patient with raised SGPT levels (*Case* 6), large areas of necrosis within the remaining liver tissue were found at necropsy. While it is known that an increase in the bile duct pressure may be a factor leading to a rise in SGPT (Braun et al., 1959) all cases had a T-tube *in situ* and we find it difficult to accept this as an aetiological factor in our patients.

Discussion

The postoperative problems encountered after hepatic resection for blunt injury to the liver are due in part to the metabolic and haematological changes that result from major hepatic resection. In addition, the effects of associated injuries and postoperative sepsis have an important bearing on the management of these patients. In particular, injuries to the chest may produce respiratory difficulty in the early postoperative period.

It is important to recognize that early signs of pulmonary insufficiency may be subtle and should be anticipated. The effects of chest injury, the presence of a thoraco-abdominal incision and incision of the diaphragm, depression of the respiratory centre as a result of head injury and possibly the result of embolization of hepatic tissue or fat embolism may all contribute to the respiratory problems. In particular it is worth emphasizing the serious combination of hypoxia and hypovolaemia which may occur in seriously injured patients (Sellors, 1961). The value of adequate blood transfusion, allowance for the effects of head injury and frequent monitoring of blood gases cannot be overstated. From the evidence in our series it would appear that most patients with injuries severe enough to necessitate hepatic lobectomy will need positive pressure ventilation and a significant proportion will require tracheostomy.

The evidence we present clearly indicates that a policy of antibiotic prophylaxis in blunt liver injury is potentially worse than ineffective. Infections are certainly not prevented by such practice nor is there any attenuation in the severity of infections when they do appear. Infections supervening on prophylaxis are always due to organisms resistant to the prophylactically administered antibiotics. We would suggest that management is best directed to the prompt diagnosis of significant infection by daily or more frequent bacteriological investigation and the intensive treatment of infection diagnosed clinically or in the laboratory. It is true that several of the metabolic and surgical complications of hepatectomy can mimic infection and the institution of treatment for infection on clinical diagnosis alone must remain a matter of delicate clinical judgement. It is, however, also true that inappropriate antibiotic therapy instituted on this basis is tantamount to prophylaxis which has its own hazards as already noted.

In general terms antibiotic policy should be to treat early infections as specifically as possible and to reserve broad spectrum therapy with such drugs as gentamicin, carbenicillin or the cephalosporins for the more complicated situations that may arise later.

The theoretical reasons for the bleeding disorders encountered after partial hepatectomy are well illustrated by our cases. Trauma to the liver is often associated with other major injuries. The liver itself is a friable vascular organ and even without haemostatic defect, profuse bleeding in these patients is not surprising. Indeed, 7 of the 8 cases in the present series required large transfusions. Stored blood is deficient in functional platelets and in labile coagulation factors V and VIII. Thrombocytopenia and coagulation factor deficiency may thus follow large transfusions of stored blood and it is possible this may even exert a positive thrombocytopenic effect (Stefanini, 1962; Ingram, 1965). In addition, the liver has important functions in maintaining normal haemostasis. It is the only site of synthesis of fibrinogen and the main site of synthesis of the vitamin-K-dependent clotting factors II, VII, IX and X and of factor V. By virtue of its reticulo-endothelial content it plays a part in clearing activated coagulation factors (Spaet et al., 1961). It also has a role in preventing excessive fibrinolysis, possibly by producing antiplasmin (Sherry, 1968). Impairment of liver function can thus result in coagulation defects and increased fibrinolysis. Depressed fibrinogen levels are a late result of severe hepatic impairment because of the relatively long half-life of circulating fibrinogen. The half-life of the activity of certain coagulation factors, e.g. factors V, VII and IX, however, is much shorter and with impaired synthesis deficiency readily occurs.

Finally, intravascular coagulation may accompany severe injuries or surgical procedures and may be aggravated by anoxia and hypovolaemia (Hardaway, 1966). Intravascular coagulation results in variable fibrinogen loss and thrombocytopenia with activation and then depletion of the labile coagulation factors V and VIII. Lysis of deposited fibrin results in increased levels of circulating fibrin degradation products and these may interfere with the polymerization of fibrin and prolong the thrombin clotting time. It should be noted, however, that FDP could conceivably be absorbed from haematomas, and raised levels alone should not be accepted as definite evidence of intravascular coagulation.

The complex nature of the coagulation defects makes specific therapy difficult and perhaps dangerous. Preparations of concentrated liver factors (factors II, VII, IX and X) are available but experience of their use is limited. The clotting factors which they contain may be more active than in their native form and their administration is best avoided if there is evidence of intravascular coagulation. The treatment of intravascular coagulation is also difficult. Theoretically, administration of heparin will arrest the condition but its early use in surgical cases is precluded. It may also be possible to treat other specific defects but therapy with concentrated coagulation factors may aggravate intravascular coagulation. Increased systemic fibrinolysis did not appear to be common after partial hepatectomy and fibrinolytic inhibitors were not used. These substances may also aggravate intravascular coagulation.

Because of the difficulties of specific therapy adequate blood replacement, particularly with fresh blood, is the mainstay of treatment. Fresh blood provides platelets and coagulation factors and is important for the prophylaxis of haemostatic defects. It is usually possible in this country to obtain fresh blood within a few hours from local donor sessions.

The low serum albumin levels recorded cannot be entirely explained on the basis of the loss of synthetic capacity of the liver as a result of tissue depletion, since the drop in serum albumin level was immediate and it has been shown that even complete cessation of albumin production only results in a 25 per cent decrease in serum level after 8 days (Martin and Neuberger, 1957). In addition, increased capillary permeability, with indirect loss of plasma proteins into the extravascular spaces, has been demonstrated in dogs after total hepatectomy, and may account for some of the postoperative fall in serum albumin levels that we have observed. Of the other factors which might account for the changes observed, the effects of infusion of large volumes of fluid, exudation from the embolization of hepatic tissue or fat embolism may all contribute to the respiratory problems. In particular it is worth emphasizing the serious combination of hypoxia and hypovolaemia which may occur in seriously injured patients (Sellors, 1961). The value of adequate blood transfusion, allowance for the effects of head injury and frequent monitoring of blood gases cannot be overstated. From the evidence in our series it would appear that most patients with injuries severe enough to necessitate hepatic lobectomy will need positive pressure ventilation and a significant proportion will require tracheostomy.

The evidence we present clearly indicates that a policy of antibiotic prophylaxis in blunt liver injury is potentially worse than ineffective. Infections are certainly not prevented by such practice nor is there any attenuation in the severity of infections when they do appear. Infections supervening on prophylaxis are always due to organisms resistant to the prophylactically administered antibiotics. We would suggest that management is best directed to the prompt diagnosis of significant infection by daily or more frequent bacteriological investigation and the intensive treatment of infection diagnosed clinically or in the laboratory. It is true that several of the metabolic and surgical complications of hepatectomy can mimic infection and the institution of treatment for infection on clinical diagnosis alone must remain a matter of delicate clinical judgement. It is, however, also true that inappropriate antibiotic therapy instituted on this basis is tantamount to prophylaxis which has its own hazards as already noted.

In general terms antibiotic policy should be to treat early infections as specifically as possible and to reserve broad spectrum therapy with such drugs as gentamicin, carbenicillin or the cephalosporins for the more complicated situations that may arise later.

The theoretical reasons for the bleeding disorders encountered after partial hepatectomy are well illustrated by our cases. Trauma to the liver is often associated with other major injuries. The liver itself is a friable vascular organ and even without haemostatic defect, profuse bleeding in these patients is not surprising. Indeed, 7 of the 8 cases in the present series required large transfusions. Stored blood is deficient in functional platelets and in labile coagulation factors V and VIII. Thrombocytopenia and coagulation factor deficiency may thus follow large transfusions of stored blood and it is possible this may even exert a positive thrombocytopenic effect (Stefanini, 1962; Ingram, 1965). In addition, the liver has important functions in maintaining normal haemostasis. It is the only site of synthesis of fibrinogen and the main site of synthesis of the vitamin-K-dependent clotting factors II, VII, IX and X and of factor V. By virtue of its reticulo-endothelial content it plays a part in clearing activated coagulation factors (Spaet et al., 1961). It also has a role in preventing excessive fibrinolysis, possibly by producing antiplasmin (Sherry, 1968). Impairment of liver function can thus result in coagulation defects and increased fibrinolysis. Depressed fibrinogen levels are a late result of severe hepatic impairment because of the relatively long half-life of circulating fibrinogen. The half-life of the activity of certain coagulation factors, e.g. factors V, VII and IX, however, is much shorter and with impaired synthesis deficiency readily occurs.

Finally, intravascular coagulation may accompany severe injuries or surgical procedures and may be aggravated by anoxia and hypovolaemia (Hardaway, 1966). Intravascular coagulation results in variable fibrinogen loss and thrombocytopenia with activation and then depletion of the labile coagulation factors V and VIII. Lysis of deposited fibrin results in increased levels of circulating fibrin degradation products and these may interfere with the polymerization of fibrin and prolong the thrombin clotting time. It should be noted, however, that FDP could conceivably be absorbed from haematomas, and raised levels alone should not be accepted as definite evidence of intravascular coagulation.

The complex nature of the coagulation defects makes specific therapy difficult and perhaps dangerous. Preparations of concentrated liver factors (factors II, VII, IX and X) are available but experience of their use is limited. The clotting factors which they contain may be more active than in their native form and their administration is best avoided if there is evidence of intravascular coagulation. The treatment of intravascular coagulation is also difficult. Theoretically, administration of heparin will arrest the condition but its early use in surgical cases is precluded. It may also be possible to treat other specific defects but therapy with concentrated coagulation factors may aggravate intravascular coagulation. Increased systemic fibrinolysis did not appear to be common after partial hepatectomy and fibrinolytic inhibitors were not used. These substances may also aggravate intravascular coagulation.

Because of the difficulties of specific therapy adequate blood replacement, particularly with fresh blood, is the mainstay of treatment. Fresh blood provides platelets and coagulation factors and is important for the prophylaxis of haemostatic defects. It is usually possible in this country to obtain fresh blood within a few hours from local donor sessions.

The low serum albumin levels recorded cannot be entirely explained on the basis of the loss of synthetic capacity of the liver as a result of tissue depletion, since the drop in serum albumin level was immediate and it has been shown that even complete cessation of albumin production only results in a 25 per cent decrease in serum level after 8 days (Martin and Neuberger, 1957). In addition, increased capillary permeability, with indirect loss of plasma proteins into the extravascular spaces, has been demonstrated in dogs after total hepatectomy, and may account for some of the postoperative fall in serum albumin levels that we have observed. Of the other factors which might account for the changes observed, the effects of infusion of large volumes of fluid, exudation from the

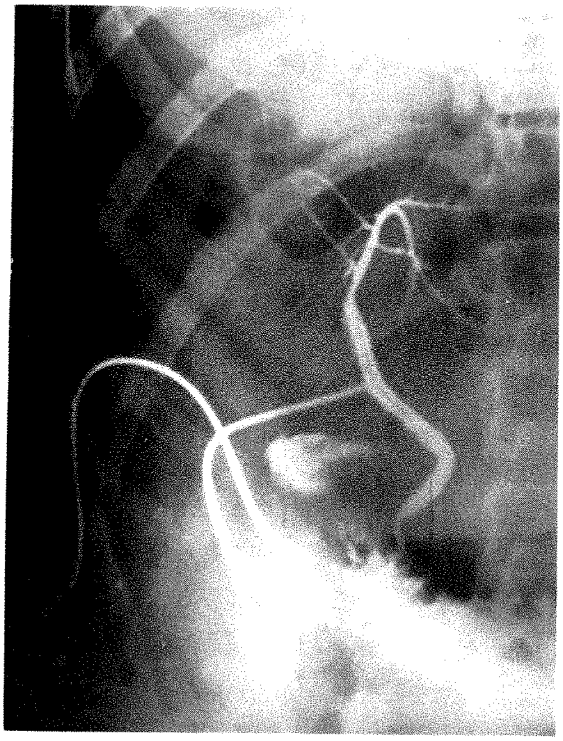


Fig. 6. T-tube cholangiogram in a jaundiced patient after partial hepatectomy showing no extrahepatic obstruction.

raw surface of the liver after operation and postoperative sepsis may be important.

Some surgeons have reported no significant change in the blood sugar level of their patients (Pack and Molander, 1960; Lin and Chen, 1965). However, we have found that hypoglycaemia can be significant following partial hepatectomy, and others (McDermott et al., 1963) have reported similar experience. Hypoglycaemia should be expected since in the fasting state blood glucose is derived directly from liver glycogen and this is seriously depleted following liver resection. Furthermore, enzyme activities related to liver glycolysis are depressed during the initial post-injury period (Weber and Cantero, 1955; Van Lancker and Sempoux, 1958).

Jaundice occurred in all our patients in the postoperative period and two patterns emerged from the study of our cases. In the patients who survived the serum bilirubin level never rose above 10 mg/100 ml and reached a peak within the first postoperative week (type I). In these cases both the conjugated and unconjugated fractions of bilirubin were elevated but the unconjugated bilirubin fractions showed the greatest rise. Haemolysis of transfused red blood cells and absorption of haematoma with increased production of bilirubin are possible causes of this rise in unconjugated bilirubin. Furthermore, minor elevations in the conjugated fractions of bilirubin may be seen in haemolytic states (Schmid, 1972). In addition to these factors, impaired hepatic uptake and defective excretion of bilirubin are known to occur after partial hepatectomy in animals (Weinbren and Billing, 1958; Wood et al., 1973). There is, however, good evidence that liver enzyme activities show only a transient decrease following partial hepatectomy (Bengmark, 1970), and the gradual fall in the plasma unconjugated bilirubin in our patients testifies to cellular recovery. There must, however, be some element of obstruction of bile outflow since bilirubinurea was detected in all our cases. T-tube cholangiography did not demonstrate any block in the extrahepatic part of the biliary ductal system so that the obstructive element must be intrahepatic in origin. This factor was of much greater importance in the severely jaundiced patients (type II) with serum bilirubin levels above 10 mg/100 ml.

In these severely jaundiced patients (type II) haemolysis could not account for the progressive rise in bilirubin levels. It has been well documented that prolonged intrahepatic cholestasis may give rise to great increases in conjugated bilirubin levels with only variable changes in the level of the serum transaminase and alkaline phosphatase (Sheldon and Sherlock, 1957). The findings in our patients are typical of severe cholestasis, and indeed histological examination of the liver remnant at post-mortem confirmed this. In addition, it should be noted that these patients not only suffered preoperative and intra-operative hypotension but were severely infected after operation, and it is known that sepsis is a cause of intrahepatic cholestasis (Fahrländer et al., 1964). Some have suggested that severe reduction in the liver cell mass may lead to engorgement, increased intrahepatic pressure and consequent pressure on small intrahepatic biliary radicals (McDermott, 1970). Others (Almersjö et al., 1969) have proposed that the postoperative jaundice may be due to increased pressure within the bile ducts. We find this difficult to accept since the presence of T-tube drainage did not prevent the development of jaundice in our patients. Bile pigment precipitation with intrahepatic cholestasis would seem to be a much more likely cause of the jaundice, and indeed some degree of postoperative cholestasis may occur in any patient who has undergone a major operation (Schmid et al., 1965). Finally, it should be noted that the presence of acute renal failure might contribute to the retention of conjugated serum bilirubin, since it has been shown that jaundiced patients with impaired renal function cannot secrete conjugated bilirubin efficiently (Wallace and Owen, 1964). Lucas et al. (1969) have shown an increased morbidity and late mortality rate with extrahepatic biliary drainage in patients with liver injury. These studies include patients with injury of varying severity and a preponderance of patients with penetrating liver wounds. The evidence against the use of T-tube drainage in major blunt injury to the liver is as yet inconclusive and we continue to advocate T-tube drainage of the common bile duct after liver resection for injury. This allows the early detection of haemobilia and regular bacteriological culture of bile and, in addition, T-tube cholangiography (*Fig.* 6) can exclude an extrahepatic obstruction in the jaundiced patient after liver resection. Jaundice alone is not an indication for reoperation, particularly if the serum proteins and other parameters of liver function are showing signs of recovery.

The remarkable regenerative capacity of the liver following major hepatic resection is well documented. It has recently been shown, using post-mortem observations, weight estimations and serial radioisotopic liver scans taken from some of the patients reported here, that liver regeneration in man commences soon after operation and progresses rapidly during the subsequent 2–3 weeks, there being little increase in the liver size thereafter (Blumgart et al., 1971).

The speed of this regenerative activity has a bearing on the metabolic activity. During regeneration much of the cellular energy is occupied with division and less is available for normal liver function. We have shown in this series of patients that liver cellular function is recovering within 2 weeks of major hepatic resection and by the sixth postoperative week is virtually normal. It should not be forgotten that many of the reports relating to the metabolic changes after liver resection are concerned with changes observed after resection for tumour. In such patients, and especially if they have large tumours, the residual healthy tissue may already have undergone some degree of compensatory hyperplasia and hypertrophy. Removal of such a tumour may produce only relatively small changes in the functional capacity of the residual liver. No such compensatory changes could have taken place before resection for injury. The striking relationship between the speed of regeneration and the consequent metabolic recovery is a factor to take into account in clinical management. In particular, we have found that routine administration of albumin in the postoperative period has not been necessary in our patients, and have noted the recovery of serum albumin levels coincident with return in function of the remaining liver.

The effects of hypoperfusion as a result of shock should not be underestimated. In particular, a rising fraction of conjugated serum bilirubin (in the presence of a patent extrahepatic biliary tree), an early rise in the alkaline phosphatase, a sustained rise in the SGPT or a continuing fall in serum protein levels after the second week should be taken as indicative of a severe degree of liver damage.

Acknowledgement

We wish to thank Professor K. Weinbren, Department of Pathology, Hammersmith Hospital, for the photomicrographs.

References

ALMERSJÖ O., BENGMARK S., HAFSTRÖM L. O. and OLSSON R. (1969) Enzyme and function changes after extensive liver resection in man. *Ann. Surg.* **169**, 111–119.

ARONSEN K. F., ERICSSON B. and PIHL B. (1969) Metabolic changes following major hepatic resection. *Ann. Surg.* **169**, 102–110.

BALASEGARAM M. (1970) Hepatic surgery, present and future. *Ann. R. Coll. Surg. Engl.* **47**, 139–158.

BENGMARK S. (1970) In: PACK G. T. and ISLAMI A. H. (ed.) *Tumours of the Liver.* London, Heinemann, p. 193.

BIGGS R. and MACFARLANE R. G. (1962) *Treatment of haemophilia and other Coagulation Disorders*, 3rd ed. Oxford, Blackwell.

BLUMGART L. H. (1973) Injuries to the liver. In: MAINGOT R. (ed.) *Abdominal Operations*, 6th ed. New York, Appleton-Century-Crofts, ch. 51.

BLUMGART L. H., LEACH K. G. and KARRAN S. J. (1971) Observations on liver regeneration after right hepatic lobectomy. *Gut* **12**, 922–928.

BLUMGART L. H. and VAJRABUKKA T. (1972) Injuries to the liver: analysis of 20 cases. *Br. Med. J.* **1**, 158–164.

BRAUN P., PAPP M. and HORVATH I. (1959) Determination of transaminase activity in dogs' serum and lymph after hepatic damage due to acute biliary obstruction. *Nature (Lond.)* **183**, 48.

CROSTHWAIT R. W., ALLEN J. E., MURGA F., BEALL A. C. jun. and DEBAKEY M. E. (1962) The surgical management of 640 consecutive liver injuries in civilian practice. *Surg. Gynecol. Obstet.* **114**, 650–654.

DENSON K. W. (1961) The specific assay of Prower-Stuart Factor and Factor VII. *Acta Haematol. (Basel)* **25**, 105–120.

DONOVAN A. J., MICHAELIN M. J. and YELLIN A. E. (1973) Anatomical hepatic lobectomy in trauma to the liver. *Surgery* **73**, 833–847.

FAHRLÄNDER H., HUBER F. and GLOOR F. (1964) Intrahepatic retention of bile in severe bacterial infection. *Gastroenterol.* **47**, 590–599.

FOSTER J. H., LAWLER M. R. jun., WELBORN M. B. jun., HOLCOMB G. W. and SAWYERS J. L. (1968) Recent experience with major hepatic resection. *Ann. Surg.* **167**, 651–658.

GIDDINGS J. C. and BLOOM A. L. (1971) A study of two methods for estimating plasma fibrinogen and the effect of epsilon aminocaproic acid and protamine. *J. Clin. Pathol.* **24**, 467–471.

HANNA W. A., BELL D. M. and COCHRAN W. (1965) Liver injuries in Northern Ireland. *Br. J. Surg.* **52**, 99–106.

HARDAWAY R. M. (1966) *Syndromes of Disseminated Intravascular Coagulation.* Springfield, Ill., Thomas.

HARDISTY R. N. and INGRAM G. I. C. (1965) *Bleeding Disorders.* Oxford, Blackwell.

INGRAM G. I. (1965) The bleeding complications of blood transfusion. *Transfusion* **5**, 1–5.

LIN T. Y. and CHEN C. C. (1965) Metabolic function and regeneration of cirrhotic and non-cirrhotic livers after hepatic lobectomy in man. *Ann. Surg.* **162**, 959–972.

LITTLE J. M. (1971) *The Management of Liver Injuries.* Edinburgh, Livingstone.

LITTLE J. M. and WILLIAMS C. W. (1969) Improved mortality in the management of liver injuries. *Br. J. Surg.* **56**, 603–610.

LLOYD-DAVIES O. V. and ANGELL J. C. (1957) Right hepatic lobectomy. Operative technique, some anatomical points, and an account of a case. *Br. J. Surg.* **45**, 113–117.

LUCAS C. E., LENAGHAN R. and WALT A. J. (1969) Biliary drainage in liver trauma. *Surg. Forum* **20**, 388–390.

MCCLELLAND R. N. and SHIRES T. (1965) Management of liver trauma in 259 consecutive patients. *Ann. Surg.* **161**, 248–257.

MCDERMOTT W. V. jun. (1970) Circulatory changes associated with major hepatic resection. *Ann. NY Acad. Sci.* **170**, 246–250.

MCDERMOTT W. V. jun., GREENBERGER N. J., ISSELBACHER K. J. and WEBER A. L. (1963) Major hepatic resection. Diagnostic techniques and metabolic problems. *Surgery* **54**, 56–66.

MARTIN N. H. and NEUBERGER A. (1957) Protein metabolism and the liver. *Br. Med. Bull.* **13**, 113–118.

MERENDINO K. A., DILLARD D. H. and CAMMOCK E. E. (1963) The concept of surgical biliary decompression in the management of liver trauma. *Surg. Gynecol. Obstet.* **117**, 285–293.

MERSKEY C., KLEINER G. J. and JOHNSON A. J. (1966) Quantitative estimation of split products of fibrinogen in human serum, relation to diagnosis and treatment. *Blood* **28**, 1–18.

MIKESKY W. E., HOWARD J. M. and DEBAKEY M. E. (1956) Injuries of the liver in 300 consecutive patients. *Int. Abstr. Surg.* **103**, 323–337.

NILEHN J. E., NILSSON I. M., ARONSEN K. F. and ERICSSON B. (1967) Studies on blood clotting factors in man after massive liver resection. *Acta Chir. Scand.* **133**, 189–195.

PACK G. T., ISLAMI A. H., HABBARD J. C. and BRASFIELD R. D. (1962) Regeneration of human liver after major hepatectomy. *Surgery* **52**, 617–623.

PACK G. T. and MOLANDER D. W. (1960) Metabolism before and after hepatic lobectomy for cancer. *Arch. Surg.* **80**, 685–692.

POLL J. G. and ROBINSON J. (1959) Assay of plasma antihaemophilic globulin (AHG) *Br. J.Haematol.* **5**, 17–23.

PROCTOR R. R. and RAPPAPORT S. I. (1961) The partial thromboplastin time with kaolin. A simple screening test for first stage plasma clotting factor deficiencies. *Am. J. Clin. Pathol.* **36**, 212–219.

QUATTLEBAUM J. K. and QUATTLEBAUM J. K. jun. (1959) Technique of hepatic lobectomy. *Ann. Surg.* **149**, 648–651.

SCHMID R. (1972) Bilirubin metabolism in man. *New Engl. J. Med.* **287**, 703–709.

SCHMID M., HEFI M. L., GATTIKER R., KISTLER H. J. and SENNING A. (1965) Benign post-operative intrahepatic cholestasis. *New Engl. J. Med.* **272**, 545–550.

SELLORS T. H. (1961) The management of chest injuries. *Thorax* **16**, 1–2.

SHARP A. A., HOWIE B., BIGGS R. and METHUEN D. T. (1958) Defibrination syndrome in pregnancy; value of various diagnostic tests. *Lancet* **2**, 1309–1312.

SHELDON S. and SHERLOCK S. (1957) Viral hepatitis with features of prolonged bile retention. *Br. Med. J.* **2**, 734–738.

SHERRY S. (1968) Fibrinolysis. *Ann. Rev. Med.* **19**, 247–268.

SPAET T. H., HOROWITZ H. I., ZUCKER-FRANKLIN D., CINTRON J. and BIEZENSKI J. J. (1961) Reticuloendothelial clearance of blood thromboplastin by rats. *Blood* **17**, 196–205.

SPEER R. J. and BORGES J. E. (1962) A convenient method for preparation of factor V deficient plasma. *J. Lab. Clin. Med.* **60**, 833–838.

STEFANINI M. (1962) Studies on the haemostatic breakdown during massive replacement transfusions. *Am. J. Med. Sci.* **244**, 298–305.

TAYLOR I. and BLUMGART L. H. (1971) Right hemihepatectomy for extensive liver injury. *Br. J. Clin. Pract.* **25**, 81–84.

VAN LANCKER J. L. and SEMPOUX D. G. (1958) Regeneration of various cellular components in rat livers after subtotal hepatectomy. *Arch. Biochem.* **77**, 129–137.

VARLEY H. (1967) *Practical Clinical Biochemistry*, 4th ed. London, Heinemann.

WALLACE D. K. and OWEN E. E. (1964) An evaluation of mechanism of bilirubin excretion by the human kidney. *J. Lab. Clin. Med.* **64**, 741–755.

WALT A. J. (1969) The surgical management of hepatic trauma and its complications. *Ann. R. Coll. Surg. Engl.* **45**, 319–339.

WEBER G. and CANTERO A. (1955) Glucose-6-phosphatase activity in regenerating embryonic and new-born rat liver. *Cancer Res.* **15**, 679–684.

WEINBREN K. (1959) Regeneration of the liver. *Gastroenterology* **37**, 657–668.

WEINBREN K. and BILLING B. H. (1956) Hepatic clearance of bilirubin as an index of cellular function in regenerating rat liver. *Br. J. Expt. Pathol.* **37**, 199–204.

WOOD C. B., KARRAN S. J. and BLUMGART L. H. (1973) Metabolic changes following varying degrees of partial hepatectomy in the rat. *Br. J. Surg.* **60**, 613–617.

Br. J. Surg. Vol. 62 (1975) 201–204

The application of the ^{99}Tc^{m} phosphate bone scan to the study of breast cancer

D. L. CITRIN, R. G. BESSENT, W. R. GREIG, N. J. McKELLAR, C. FURNIVAL AND L. H. BLUMGART*

SUMMARY

Comparison of the gamma camera bone scan and radiological survey in 190 patients with breast cancer has confirmed the superiority of the bone scan in the positive diagnosis of skeletal metastases. In 47 patients with known (X-ray positive) bony metastases the scan was positive in all but 2, and in 24 (50 per cent) the scan showed more lesions than the X-ray had indicated. In 60 patients with a clinical suspicion of bone metastases but negative X-rays, the scan was positive in 29 (48 per cent). Eighty-three patients with primary breast cancer were studied at the time of initial presentation. All had a normal radiographic skeletal survey but 24 (27 per cent) had scan evidence of occult metastases. It is concluded that a bone scan is indicated in all patients with breast cancer where skeletal metastases are suspected.

Repeated bone scans may introduce new therapeutic possibilities, by providing an earlier objective index of progression of metastatic disease and also by providing a quantitative method of assessing the response to therapy.

BONE scanning is a valuable diagnostic aid in the detection of skeletal metastases (Charkes et al., 1968) and has shown great promise in the study of breast cancer (Galasko et al., 1968). Because of the recent introduction of the ^{99}Tc^{m} phosphates, high quality bone scans are now available in all hospitals with scanning facilities (Citrin, Greig et al., 1974). In this paper we record our experience of the ^{99}Tc^{m} bone scan and radiographic skeletal survey in 190 patients with breast cancer.

Materials and methods

One hundred and ninety female patients with breast cancer and 70 control subjects were studied. The breast cancer patients may be divided into three main groups:

1. Patients with known bony metastases (X-ray positive) who were scanned to allow us to develop and validate our technique (47 patients).
2. Patients in whom there was a clinical suspicion of metastases but no definite lesion seen on X-rays (60 patients).
3. Patients scanned at the time of initial presentation and primary treatment (83 patients).

Each patient was scanned 4 hours after the intravenous injection of 10 mCi of ^{99}Tc^{m} phosphate, using a Nuclear Enterprises Scinticamera IV gamma camera. All the scans were recorded on Polaroid film. Multiple overlapping views of the skeleton were obtained with the patient either seated or standing (for pelvic views). Twelve views were obtained: right and left lateral skull (2 views), cervical, dorsal and lumbar spine (3 views), right and left shoulders, and proximal humeri (2 views), sternum and anterior ribs (1 view), right and left anterior and posterior pelvis with proximal femora (4 views). Spinal pictures were taken with 300 000 counts and all other pictures with 200 000. In some patients a more limited examination (restricted to known tumour-bearing areas) was made.

Table I: RESULTS OF SCAN AND X-RAY IN PATIENTS WITH KNOWN BONY METASTASES

	Total no.	Scan positive	Scan negative	Scan suspicious
X-ray positive	47	45	2	0
X-ray negative	0	0	0	0
X-ray suspicious	0	0	0	0
Total	47	45	2	0

Table II: RESULTS OF SCAN AND X-RAY IN PATIENTS WITH CLINICAL SUSPICION BUT NO DEFINITE METASTASES ON X-RAY

	Total no.	Scan positive	Scan negative	Scan suspicious
X-ray positive	0	0	0	0
X-ray negative	59	28	26	5
X-ray suspicious	1	1	0	0
Total	60	29	26	5

Table III: RESULTS OF SCAN AND X-RAY IN PATIENTS WITH PRIMARY BREAST CANCER

	Total no.	Scan positive	Scan negative	Scan suspicious
X-ray positive	0	0	0	0
X-ray negative	81	21	49	11
X-ray suspicious	2	1	1	0
Total	83	22	50	11

In all the patients a radiological skeletal survey was obtained within 1 week of the scan, comprising anteroposterior and lateral views of the skull, anteroposterior and lateral views of the cervical, dorsal and lumbar spine, chest with rib views and pelvis. The scans and X-rays were independently read by a nuclear medicine physician and a consultant radiologist respectively. Results were recorded as positive, negative or suspicious for metastases. The results of the two investigations were then compared.

---

* University Departments of Medicine and Surgery, Departments of Nuclear Medicine and Radiology, Glasgow Royal Infirmary, and Western Regional Hospital Board, Department of Clinical Physics and Bio-engineering, Glasgow.

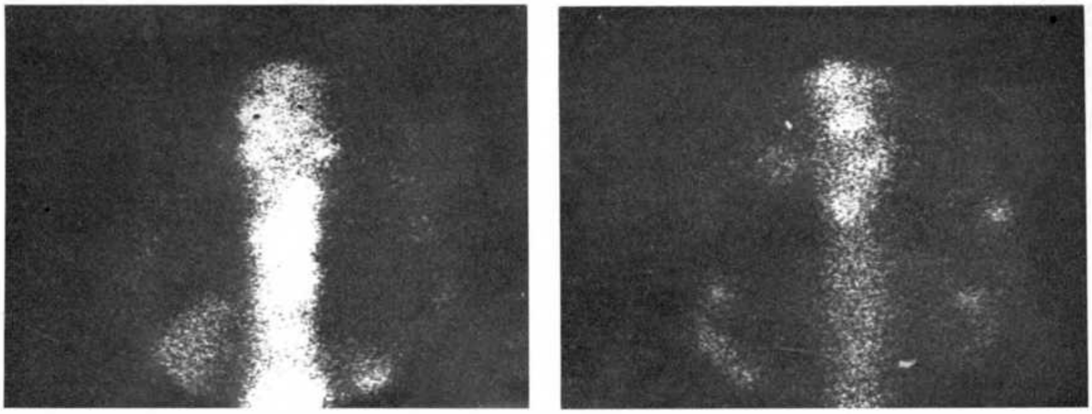


Fig. 1. Case with X-ray-positive metastases in T10 and T11; remainder of X-ray skeletal survey negative. *a*. Scan of dorsolumbar spine shows lesions throughout the lower dorsal spine. *b*. Anterior ribs and sternum are extensively involved.

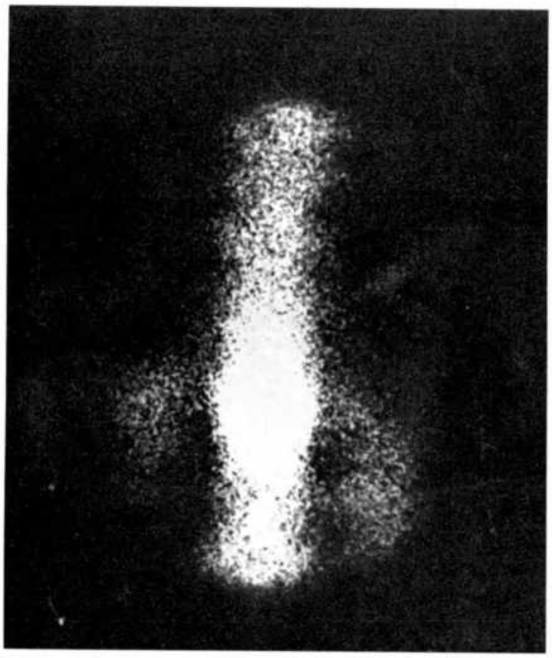


Fig. 2. Scan of a 44-year-old patient who had undergone mastectomy 2 years before. She presented with back pain, but an X-ray was negative. A lesion was seen in the lower dorsal spine on a scan. One week's radiotherapy relieved the pain.

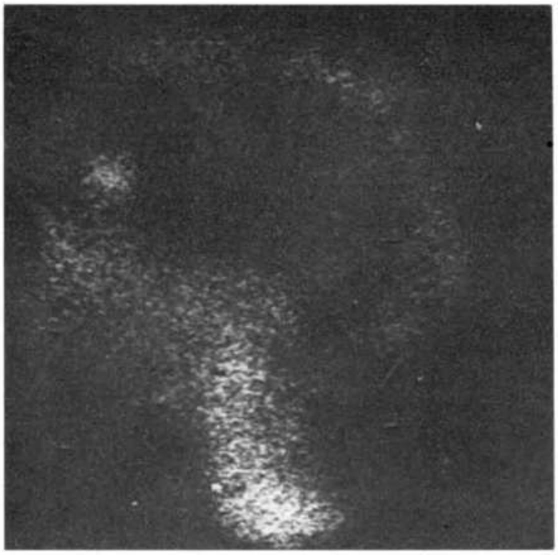


Fig. 3. Scan of a 50-year-old patient with cancer of the left breast (clinically stage II) at the time of presentation. X-rays taken at this time were negative. The scan shows tumour of the left frontal bone, which was confirmed radiologically 6 months later.

Seventy control subjects were scanned using an identical technique to that employed in the breast cancer patients. The controls were postmenopausal females and male patients over the age of 35 with no history or evidence of malignant disease. The control scans were reported without knowledge of the clinical history.

Results

The results are summarized in *Tables I–III*. In all but 2 of the 47 patients with radiographically demonstrable bony metastases the scan showed corresponding abnormalities (*Table I*). In 24 (50 per cent) the scan clearly showed metastases to be more widespread than the X-ray had suggested (*Fig*. 1). The two X-ray-positive scan-negative cases are of interest in that both had had spinal metastases for over 5 years. X-rays showed healed sclerotic lesions, and we have interpreted the negative scans as indicating inactive disease.

In 60 patients, despite the clinical suspicion of metastatic disease, the X-rays were not confirmatory (*Table II*). Twenty-nine of these patients (48 per cent) had positive bone scans, and in many of these cases the presence of metastatic tumour has been confirmed by the clinical course or subsequent studies (*Fig*. 2). Five patients had areas on the scan which were considered suspicious but not diagnostic of metastases, and follow-up studies are being carried out. The remaining 26 patients had normal bone scans.

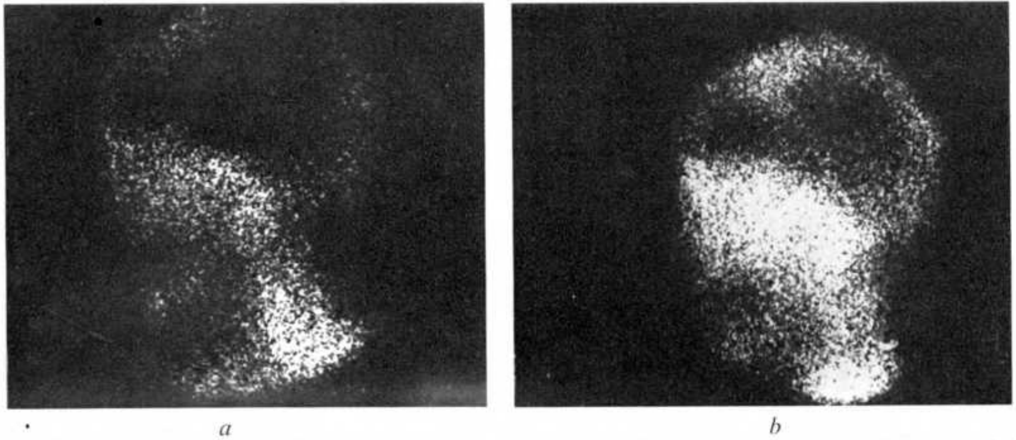


Fig. 4. Scans of a 62-year-old patient with stage I breast cancer (*a*) at the time of mastectomy and (*b*) 6 months later, when the patient was clinically well. Both scans show a lesion of the left frontoparietal bone which has progressed. X-rays were consistently negative on both occasions.

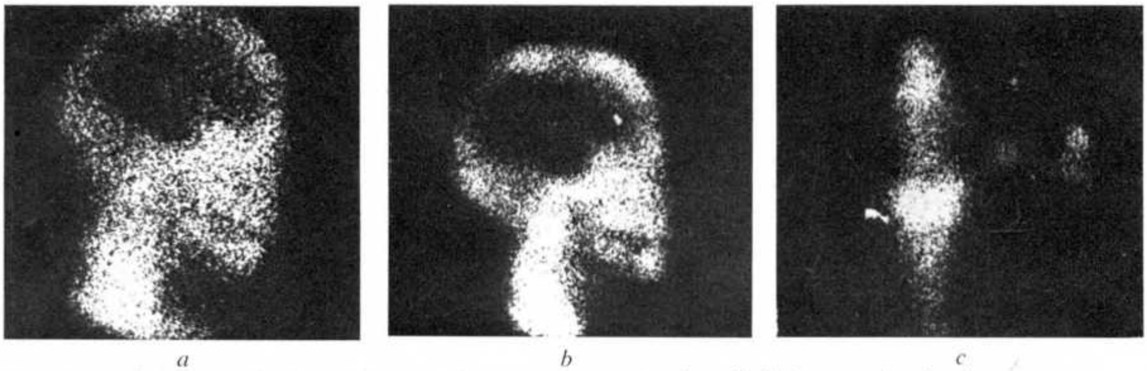


Fig. 5. Scans of a 49-year-old patient with stage II breast cancer (*a*) at the time of initial presentation showing metastases of the skull, and (*b*) and (*c*) 6 months later, when the patient was clinically well and radiologically negative. There are lesions in the skull and left clavicle (tumour in clavicle was scan negative at the time of presentation).

Eighty-three patients with primary breast cancer were scanned and X-rayed as part of their initial assessment (*Table III*). None of these patients had definite metastases visible on the radiographic skeletal survey. Twenty-two (27 per cent) were considered to have changes on the scan diagnostic of metastatic deposits, and in a further 11 cases (14 per cent) there were changes suspicious but not entirely diagnostic of metastases. In 4 patients to date X-rays have confirmed the presence of metastatic tumour at sites initially indicated by the bone scan (*Fig*. 3). In 11 patients serial scans have documented consistent abnormalities which in several patients have clearly progressed (*Figs*. 4, 5).

In 2 control subjects, abnormalities were noted which could be interpreted as metastatic deposits. In one subject the X-ray was normal and in the other the X-ray demonstrated a localized concentration of bone in the area indicated by the scan. Both control subjects remain well 1 year after scanning.

Discussion

Our preliminary results (Citrin, Greig et al., 1974) and those presented here have led us to conclude that the ^{99}Tc^{m} phosphate scan allows earlier and more accurate diagnosis of skeletal metastases than the conventional X-ray. In all the patients with X-ray-positive metastases (with the exception of 2 with probably inactive lesions) scanning confirmed the presence of metastases and in 24 (50 per cent) showed additional lesions not yet visible on the X-ray. Forty-eight per cent of patients with a clinical suspicion of metastases and 27 per cent of primary breast cancer patients were also shown by scanning to have metastases not demonstrable in the radiographic skeletal survey. The incidence of 'false positives' in the control group was acceptably low (3 per cent).

The scan is well tolerated by the patient; she does not need to undress and there is less physical manipulation than with conventional radiography. We have recently increased the isotope activity given; we now routinely give 15 mCi of ^{99}Tc^{m}-labelled ethane hydroxydiphosphonate (EHDP), which appears to be the best of the available compounds (Citrin et al., 1975). Scanning time is no longer than 30 minutes in any one patient and high quality bone scans are consistently obtained.

The technique of bone scanning is particularly appropriate to breast cancer because 85 per cent of patients who die from this disease have bone metastases (Jaffe, 1958). Against this background a detailed study of patients with primary breast cancer is currently in progress at Glasgow Royal Infirmary. Patients are scanned before commencing treatment and at 6-monthly intervals thereafter. The final results of this study will be published at a future date. Of interest at the present time is the finding that the incidence of X-ray-negative patients with positive scans in our group was 27 per cent, which is similar to that previously reported by Galasko et al. (1968). Clearly, the bone scan may provide valuable clinical information in the initial assessment of the primary case. The use of this information in relation to management of the individual case and the formation of valid groups for future clinical trials is being assessed.

Since EHDP is convenient, non-toxic and imposes only a small radiation burden (Citrin et al., 1975), serial scanning is now feasible. Scans repeated at intervals have demonstrated progressive metastases in several patients who were previously scan-negative and who remain entirely symptom-free following mastectomy, and it appears that there is emerging a group of patients in whom these lesions can now be identified as they occur by using serial scans. In this group the possibility of treating these demonstrable lesions at an early stage (even before symptoms develop) must now be considered. The conclusion that chemotherapeutic and hormonal methods are capable of inducing only a temporary remission of bone metastases is drawn from experience of metastases demonstrable by radiographic methods, and it seems unwarranted to conclude at the present time that the same result would necessarily be found in the treatment of early lesions, demonstrated by scanning but not yet visible on the X-ray. It is possible that asymptomatic metastases could be eradicated by commencing treatment at this early stage.

It has previously been suggested that the bone scan may provide a method of assessing response to therapy (Galasko and Doyle, 1972). For this purpose we have developed a rapid inexpensive method of quantifying tumour activity using the bone scan. The technique of quantitative bone scanning offers great promise as a research tool by providing an accurate method of assessing the effects of therapy on metastases which may be asymptomatic and radiologically invisible (Citrin, Bessent et al., 1974).

Our studies over the past 18 months suggest that this area may well represent the most important therapeutic application of bone scanning in breast cancer.

References

CHARKES N. D., YOUNG I. M. and SKLAROFF D. M. (1968) The pathologic basis of the strontium bone scan. Studies following administration of strontium chloride ^{85}Sr and strontium nitrate ^{85}Sr. *JAMA* **206**, 2482–2488.

CITRIN D. L., BESSENT R. G., TUOHY J. B., ELMS S. T., MCGINLAY E., GREIG W. R. and BLUMGART L. H. (1975) A comparison of phosphate bone scanning agents in normal subjects and patients with malignant disease. *Br. J. Radiol.* In the press.

CITRIN D. L., BESSENT R. G., TUOHY J. B., GREIG W. R. and BLUMGART L. H. (1974) Quantitative bone scanning: a method for assessing response of bone metastases to treatment *Lancet*, **1**, 1132-1133.

CITRIN D. L., GREIG W. R., CALDER J. F., BESSENT R. G., TUOHY J. B. and BLUMGART L. H. (1974) Preliminary experience of bone scanning with ^{99m}Tc-labelled polyphosphate in malignant disease. *Br. J. Surg.* **61**, 73–75.

GALASKO C. S. B. and DOYLE F. H. (1972). The response to therapy of skeletal metastases from mammary cancer: assessment by scintigraphy. *Br. J. Surg.* **59**, 85–88.

GALASKO C. S. B., WESTERMAN B., LI J., SELLWOOD R. A. and BURN J. I. (1968) Use of the gamma camera for early detection of osseous metastases from mammary cancer. *Br. J. Surg.* **55**, 613–615.

JAFFE H. L. (1958) *Tumors and Tumorous Conditions of Bone and Joints.* Philadelphia, Lea & Febiger.

Br. J. Surg. Vol. 62 (1975) 205–206

Cystic thyroid nodules

MICHAEL K. G. MA AND G. B. ONG*

SUMMARY

Among 300 patients with thyroid nodules subjected to a needle drill biopsy, 62 were found to contain cystic lesions. Analysis of these 62 cases showed that in 17 the swelling had completely disappeared after the biopsy. The remaining 45 had residual or recurrent swellings. Operative treatment was carried out in 35, which consisted of 28 (80 per cent) nodular goitres, 6 (17·1 per cent) adenomas and 1 (2·9 per cent) carcinoma.

ABOUT 15 per cent of all thyroid nodules are cystic (Crile, 1966). The contents may vary from thick brownish colloid material to thin pale fluid. Clinically they present as solitary nodules either of recent onset and rapid growth or with a history of long duration with little fluctuation in size. Regardless of the mode of development, these cystic nodules are usually medium-sized with a diameter of about 2–5 cm and hard in consistency. They invariably show poor uptake of radioactive I_2 in the thyroid scan. Hence they stay high on the list for operative treatment because of the risk of malignancy. However, when the nodules are excised the majority of them turn out to be benign lesions. There is a paucity of reports in the literature on the incidence of carcinoma in cystic thyroid nodules. Preoperative needle biopsy is still a controversial practice and performed only in a selected group of patients. We set out to study the usefulness of such a procedure in the management of thyroid cyst and in obtaining early histological diagnosis.

Materials and methods

In the past 3½ years 300 drill biopsies of the thyroid gland have been performed in the Surgical Thyroid Clinic, University of Hong Kong. Patients selected for study included those presenting with either a solitary nodule or a multinodular swelling with poor radioactive iodine uptake in the scan. A high speed pneumatic drill was used. It has a needle of 1·5 mm internal diameter and is driven by compressed air at 5 kg/cm². Under local anaesthesia a small skin incision was made and the needle was inserted into the centre of the nodule. After it had penetrated the thyroid capsule, it was disconnected from the machine and withdrawn with mild suction. Whenever fluid was aspirated an attempt was always made to empty all the contents by gentle pressure on the gland. The fluid was measured and sent for cytological study. The incision was then covered with an Elastoplast dressing and the patient was discharged.

Of the 300 patients studied, 62 were found to have cystic lesions containing fluid of various character and quantity. There was thin yellowish fluid in 10, dark brownish fluid in 34 and thick colloid material in 18 (*Table I*). The amount ranged from 1 to 60 ml with an average of 8 ml.

These 62 patients were followed up regularly in the Thyroid Clinic. In 17 (27·4 per cent) the swelling completely disappeared and no further surgical intervention was indicated. However, they were all examined on a monthly basis in case of further development. Thirty-five (56·5 per cent) of the 62 patients were subsequently operated upon because of recurrent or residual swelling. Of these, 28 (80 per cent) were nodular goitres, 6 (17·1 per cent) were adenomas and only 1 carcinoma (*Table II*). The remaining 10 patients had some residual swelling in the neck but they refused operative treatment. However, they have been followed up for periods of 2 months to 3½ years and are all in good health with no signs of malignancy.

Table I: TYPE OF FLUID ASPIRATED IN 62 PATIENTS

Type	No. of cases
Thin yellow fluid	10
Thick colloid material	18
Dark brownish fluid	34

Table II: RESULTS OF DRILL BIOPSY IN 62 PATIENTS

Result	No. of cases
Nodule subsided	17
Residual swelling with no operation	10
Residual or recurrent swelling with operation	35
Nodular goitre	28 (80%)
Adenoma	6 (17·1%)
Papillary carcinoma	1 (2·9%)

Discussion

Needle biopsy of the thyroid gland has long been a controversial practice. It is only occasionally performed in apparently benign lesions because of the potential risk of tumour dissemination. Since the introduction of the high speed pneumatic drill, Deeley and Pollock (1966) have successfully used it to biopsy enlarged lymph nodes, lung, thyroid, breast and various soft tissue tumours. Risk of cancer dissemination was shown by Burn et al. (1968) to be low. We have therefore used the drill to biopsy 300 patients with thyroid swellings. Patients selected for the study included those presenting with a solitary nodule, a multi-nodular swelling with a 'cold' area in the thyroid scan or non-toxic diffuse swellings. One of the aims of this study was to evaluate the management of a cystic thyroid nodule by aspiration. If such cysts can be treated by simply emptying the contents without risk of leaving behind a carcinoma, then a large number of unnecessary operations can be avoided.

---

* Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong.

Sixty-two patients in this series were found to have cystic thyroid nodules. The cysts contained fluid of various quality and quantity which was aspirated by a high speed pneumatic drill. The character of the fluid had no significant bearing on the nature of the lesion. In 17 the swelling completely subsided with no recurrence. We chose to postpone operative treatment of these patients and to follow them up at monthly intervals. In 10 there were some residual swelling or recurrence after the drill biopsy but the patients refused operation. Both groups of patients have now been followed up for periods of 2 months to 3½ years. So far none of them has shown any signs that warrant an early exploration. In the remaining 35 of the 62 patients operation was carried out, the indication being residual or recurrent swelling. Of these, 28 (80 per cent) had nodular goitre, 6 (17·1 per cent) had adenoma and only 1 patient (2·9 per cent) had a papillary carcinoma. If we assume the cystic lesions that disappeared after aspiration to be benign, then the incidence of carcinoma in cystic thyroid nodules was 1·9 per cent. Crile (1966) treated 58 cases of thyroid cysts with needle aspiration and encountered no malignant tumour. It would appear that such cystic lesions of the thyroid gland, whether solitary or multinodular, and which routinely show poor uptake of radioactive iodine in the scan, could well be safely managed by this simple method. A preoperative drill biopsy would serve as both a diagnostic and therapeutic procedure. It is safe and was well tolerated by our 62 patients without any complication. Also, if a careful cytological examination were done on every sample of cyst contents, there should be no difficulty in diagnosing the small proportion of cases which truly warrant an operation.

References

BURN J. I., DEELEY T. J. and MALAKER K. (1968) Drill biopsy and dissemination of cancer. *Br. J. Surg.* **55**, 628–631.

CRILE G. jun. (1966) Treatment of thyroid cyst by aspiration. *Surgery* **59**, 210–212.

DEELEY T. J. and POLLOCK D. J. (1966) Experience with a high speed pneumatic drill biopsy machine. *Br. J. Cancer* **20**, 442–447.

Br. J. Surg. Vol. 62 (1975) 207–214

Thyroid cancer: twenty years' experience in a general hospital

D. J. CAMPBELL AND R. H. SAGE*

SUMMARY

Twenty years' experience of thyroid cancer in a district general hospital has been reviewed. Its incidence, prognosis and natural history have been studied. Particular attention has been focused on the relationship of malignant to benign goitre. The relevance of this to the treatment of 'apparently benign goitre' is discussed.

Clinical evidence is presented supporting the hypothesis that differentiated thyroid carcinoma evolves from a solitary focus through a multinodular form before presenting the picture of a frankly malignant locally invasive cancer.

An increase in the incidence of papillary carcinoma is confirmed.

CANCER of the thyroid is a rare disease which in the Birmingham region has an incidence of 2·0 females to 0·6 males per 100 000 of the population (*Table I*). It constitutes only 0·7 per cent of all cancers in the female and 0·2 per cent in the male (Waterhouse, 1974). In view of this, it is not surprising that the majority of series reporting thyroid cancer originate from either regional cancer centres or individuals renowned as thyroid surgeons. The selection applied to these series favours carcinoma (Crile and Dempsey, 1949) and consequently they do not reflect the experience of general surgeons nationally.

Table I: INCIDENCE OF THYROID CANCER BY AGE IN THE BIRMINGHAM REGION DURING 1960–5

Age	M	F	Age	M	F	Age	M	F
0–4	0·0	0·0	35–39	0·3	1·4	70–74	2·8	6·0
5–9	0·0	0·0	40–44	0·3	2·2	75–79	5·5	7·8
10–14	0·0	0·2	45–49	0·7	2·1	80–84	2·8	10·4
15–19	0·3	0·1	50–54	1·2	2·7	85–89	5·3	11·2
19–24	0·0	0·4	55–59	1·3	2·8	90–94	0·0	16·4
25–29	0·0	1·1	60–64	1·9	4·0	95+	0·0	0·0
30–34	0·3	1·6	65–69	2·0	5·2	All ages	0·6	2·0

Incidence rates per 100 000 of the population. Total number of cases of cancer, 88 males and 290 females.
M, Male; F, Female.

Table II: CLASSIFICATION OF PRIMARY THYROID MALIGNANCIES BY HISTOLOGICAL TYPE (1953–73)

Type:	No. of cases:
Anaplastic	17
Follicular	11
Papillary	10
Mixed papillary-follicular	6
Medullary	2
Hurthle-celled	2
Reticulum-celled sarcoma	2
Squamous-celled carcinoma	1
Lymphoma	1
Not classified	2
Total	54

The identification of a malignant goitre amidst numerous benign or apparently benign goitres has always been a problem facing general surgeons. Whilst some cancers are readily diagnosed, others present in the guise of benign goitres. This latter group requires further elucidation as the literature abounds with conflicting evidence concerning the cancer risk in apparently benign goitres. This is the result of a wide variation in case selection and depends on whether patient sampling occurs in goitrous or non-goitrous areas (Wilson, 1973).

The present study is based on the experience of thyroid cancer in a district general hospital during the period 1953–73. Attention has been focused primarily on the incidence of thyroid cancer in surgical practice. Its relationship to benign goitre, particularly the solitary nodule and non-toxic goitre, has been clarified. In addition, the natural history of thyroid cancer has been considered with particular reference to its response to treatment. It is felt that in this unselected group of patients is mirrored the experience of the vast majority of general surgeons. The Birmingham region does not include any areas of endemic goitre.

Clinical material

Fifty-four primary thyroid malignancies have been reviewed. These were diagnosed and treated at Selly Oak Hospital, Birmingham, between 1953 and 1973 and have been under constant supervision following initial diagnosis. All patients subjected to thyroidectomy during this same period have been similarly studied.

In every case the initial histological diagnosis has been verified by re-examination of the original slides. 'Representative sections' have been employed in both surgical and post-mortem studies. No 'whole organ' sections were prepared. The histological classification employed is based on the terminology of Meissner and Warren (1969).

Where appropriate, figures relating to thyroid cancer in the entire Birmingham region have been obtained from the Regional Cancer Registry.

Incidence

During the period 1953–73, 1058 thyroidectomies were performed at Selly Oak Hospital. In 45 of these cases a diagnosis of primary carcinoma was confirmed; an overall operative incidence of 4·25 per cent. Nine primary carcinomas, not treated surgically, were verified at post-mortem, having been undiagnosed clinically or considered inoperable. Three secondary thyroid carcinomas were encountered during the same period. Classification of primary growths by histological type is shown in *Table II*. *Fig.* 1 shows the overall age distribution at presentation.

---

* Selly Oak Hospital, Birmingham.

A consideration of the carcinomas in females shows a marked difference in the age distribution of differentiated and anaplastic growths (*Fig.* 2). Differentiated carcinomas first appear during the teens (postpubertal rise) to reach a peak between the ages of 45–55 years (menopause). There is then a gradual decline in the postmenopausal period. In contrast, anaplastic tumours exhibit a markedly increased incidence in the perimenopausal period, reaching a peak at 70 years. A similar but less marked age differential is recorded in the male.

The aetiological significance of these findings is unclear. Thyroid-stimulating hormone is known to be important in the development of differentiated thyroid carcinomas (Taylor, 1969a) and may be responsible for this distinctive age distribution. The accurate determination of physiological variations in the concentration of thyroid-stimulating hormone is not possible with present assay techniques (Jacobs and Lawton, 1974). The aetiology of thyroid carcinoma will become clearer when improved techniques allow an assessment of the effect of puberty and the menopause on the output of thyroid-stimulating hormone.

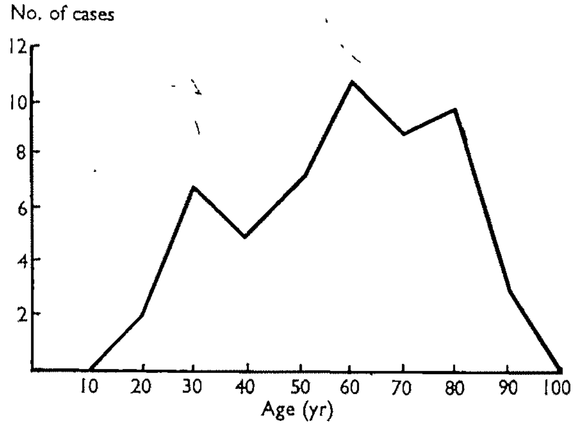


Fig. 1. Distribution by age of all thyroid cancers presenting at Selly Oak Hospital during the period 1953–73.

Increase in the incidence of papillary carcinoma

An increase in incidence of papillary carcinoma has been observed. This is most marked in the male, but a gradual rise has also been observed in the female. The percentage distribution of papillary carcinoma for 3-year periods during 1960–71 is recorded in *Table III*. The figures shown are those for the Birmingham region as they give a clearer indication of the trend than those obtained purely for Selly Oak Hospital. They confirm previous reports in the American literature (Beahrs et al., 1951; Crile, 1971). Papillary carcinoma is known to be associated with increased intake of iodine (Doniach, 1969). In the British Isles iodized table salt accounts for only 1·5–2·0 per cent of the total salt market. This, nevertheless, represents a sixfold increase when compared with the level of 1930 (Wenlock, 1974).

Diagnosis at presentation

In 21 patients (38·9 per cent) a correct diagnosis was possible on clinical grounds alone. These were invariably rapidly progressive anaplastic tumours, which did not present diagnostic problems. Nineteen of these patients have since died of their disease.

The remaining 33 carcinomas (61·1 per cent), viewed with varying degrees of clinical suspicion, were categorized as shown in *Table IV*. These categories afford clinical camouflage and it is therefore important to know the percentage of each group that is likely to be malignant. In this way an appropriate degree of clinical suspicion can be brought to bear in individual

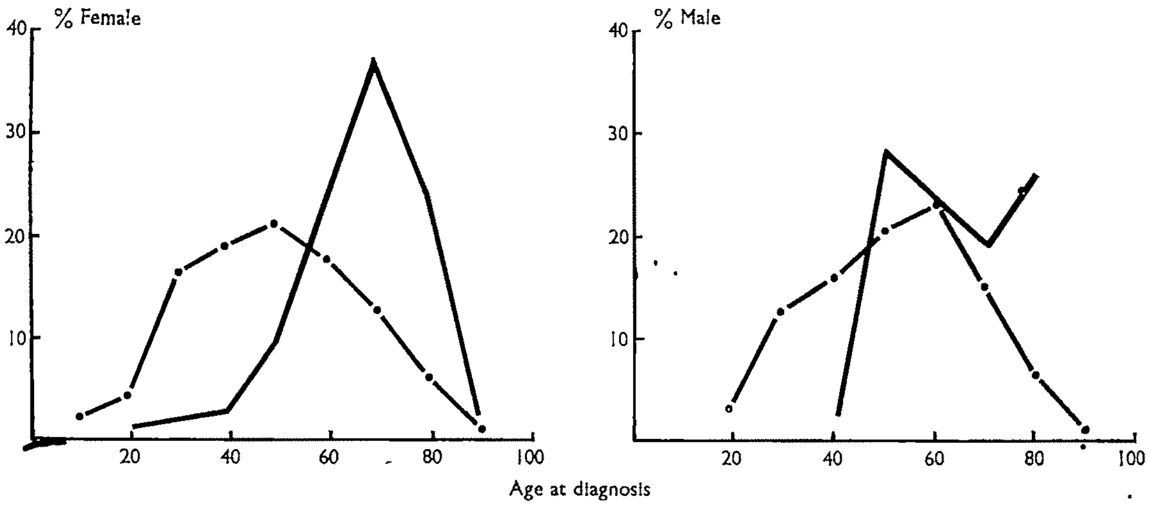


Fig. 2. Distribution by age (%) and sex of differentiated (· — ·) and undifferentiated (——) thyroid cancers in the Birmingham region.

cases. The percentages given in *Table V* are for those carcinomas that were not diagnosed clinically.

It is felt that the degree of selection applied to these goitres is neither more nor less than that applied in any other general surgical unit. Consequently, although these figures do not represent the incidence of carcinoma in toxic and non-toxic goitre amongst the general population they are figures having an important significance in surgical practice.

Solitary nodules

Eight of the clinically undiagnosed carcinomas presented in the form of a solitary nodule. They had been present for an average of 23 months (range, 1 month to 5 years) and were most common in the female (F : M ratio, 5 : 3). They presented at all ages, but most frequently in the 30–40 age group (average, 43 years). Two hundred and ninety-eight clinically solitary nodules were excised during the same period, giving a carcinoma incidence amongst excised solitary nodules of 2·7 per cent. Six nodules were well differentiated carcinomas, the remaining 2 being medullary (*Table VI*). Two of the well-differentiated growths showed evidence of early local invasion.

All solitary nodule carcinomas responded remarkably well to treatment. This involved subtotal resection of the affected lobe and, in one instance, resection of the isthmus. Two patients with evidence of local spread were additionally treated with suppressive doses of thyroxine, one of them also receiving local external irradiation. All these patients are alive, with no evidence of local or disseminated recurrence (*Table VII*). Average follow-up is 5 years 9 months, with a range of 1–15 years.

Multinodular goitre

Eighteen of the undiagnosed carcinomas presented as non-toxic multinodular goitres. They were selected for surgery on the usual clinical grounds. During the same period 141 non-toxic multinodular goitres were excised, giving a carcinoma incidence of 12·8 per cent. When all excised non-toxic goitres are considered together this figure becomes diluted to 8·7 per cent.

In contrast to solitary nodules the majority of these goitres had been present for many years, with an average of 6 years and 8 months. They therefore present later in life, the average age at presentation being 55, and predominantly in females (F : M ratio, 8 : 1).

These patients do consistently worse than those with solitary nodules. Six died of disseminated carcinoma, with a longest survival time of 6 years. Four patients are still receiving treatment for metastatic disease.

In 6 patients carcinoma supervened on a long-standing goitre (more than 10 years). As a group, these responded badly to treatment. Three died of disseminated disease, while 2 others have developed both local and distant metastases.

Toxic goitre

Three toxic goitres were found to contain carcinoma. Two of these were removed surgically, while the third

Table III: CHANGING INCIDENCE OF PAPILLARY CARCINOMA IN THE BIRMINGHAM REGION (1960–71)

	Incidence of papillary carcinoma (%)	
Period	Male	Female
1960–62	11·1	28·7
1963–65	29·0	30·2
1966–68	25·0	31·2
1969–71	44·7	39·6

Percentages are of total thyroid cancers.

Table IV: CLINICAL DIAGNOSIS APPLIED TO THYROID CANCER AT PRESENTATION

Carcinoma diagnosed clinically		21
Carcinoma undiagnosed clinically		29
Solitary nodule	8	
Non-toxic multinodular	18	
Non-toxic diffuse	1	
Toxic goitre	2	
Post-mortem diagnosis		4
	Total	54

Table V: PERCENTAGE OF MALIGNANCY AMONGST APPARENTLY BENIGN GOITRES

Type of goitre	Total no. 1953–73	Malignant No.	Malignant %
Solitary nodule	298	8	2·7
Non-toxic multinodular goitre	141	18	12·8
Non-toxic diffuse goitre	77	1	1·3
All non-toxic goitres	218	19	8·7
Toxic goitre	482	2	0·4

Table VI: TYPES OF THYROID CANCER FOUND IN SOLITARY NODULES AND MULTINODULAR GOITRE

Type of cancer	Solitary nodules	Non-toxic multinodular
Papillary	1	4
Follicular	2	6
Mixed papillary-follicular	3	1
Anaplastic	0	4
Medullary	2	0
Others	0	3*
Total	8	18

* One lymphoma, 2 Hurthle-celled.

Table VII: NATURAL HISTORY AND PROGNOSIS OF DIFFERENTIATED THYROID CARCINOMA RELATED TO CLINICAL STAGING

	Single→ nodule Stage 1	Multinodular→ Stage 2	Frankly malignant Stage 3
Local invasion at presentation (%)	25	50	90
Distant spread at presentation (%)	0	17	24
Result of treatment	Excellent	Fair	Bad
5-Year survival (%)	100	71	15
10-Year survival (%)	100	70	10

Table VIII: SURVIVAL FIGURES BY SEX FOR ALL THYROID CANCER

Sex	No. of cases	5-Year survival (%)	10-Year survival (%)
Female	42	57	52
Male	12	25	20

was discovered at post-mortem, the patient having died of thyrotoxic heart disease. Two were papillary, and the other a mixed follicular-papillary type.

The carcinoma incidence of 0·4 per cent in excised goitres is similar to the 0·354 per cent of Hurxthal and Heinemann (1958). Olen and Klinck (1966) reported an incidence of 2·5 per cent amongst hyperthyroid glands.

Results of treatment

The effect of age and sex on survival

Results of treatment for thyroid carcinoma in the female are significantly better than those obtained in the male. Female 10-year survival figures are better than those achieved at 5 years in the male (*Table VIII*). The age at presentation also exerts a marked influence on survival, as shown in *Table IX*. Patients with carcinoma presenting after 60 fare significantly worse than those with carcinoma occurring earlier. This applies equally to both sexes. It would appear, however, that females are selectively protected until they reach the postmenopausal period (*Table X*). Their good prognosis before this is responsible for the good overall survival figures for carcinoma presenting at an early age.

The effect of histological type of survival

The biological individuality of the various histological types of thyroid carcinoma has been confirmed by both pathological and epidemiological studies (Cuello et al., 1969). The difference in morbidity and mortality amongst the patients treated in the present series verifies this (*Table XI*).

Table IX: COMBINED MALE AND FEMALE SURVIVAL FIGURES BY AGE FOR ALL THYROID CANCER

Age at presentation	No. of cases	5-Year survival(%)	10-Year survival (%)
<30	4	100	100
30–60	22	75	64
>60	28	18	9

Table X: FEMALE SURVIVAL FIGURES BY AGE FOR ALL THYROID CANCER

Age at presentation	No. of cases	5-Year survival (%)	10-Year survival (%
<30	3	100	100
30–60	16	92	87·5
>60	23	21	10

Table XI: RESULTS OF TREATMENT IN FOUR HISTOLOGICAL TYPES OF PRIMARY THYROID CANCER

Type of cancer	No. treated	Tumour deaths	Non-tumour deaths	Alive with recurrence	Recurrence-free
Papillary	8	1	0	1	6
Follicular	10	3	1	2	4
Mixed papillary-follicular	5	0	0	1	4
Anaplastic	13	11	0	2	0

Papillary: Eight patients received treatment for papillary carcinoma. Two untreated carcinomas were discovered incidentally in patients dying of unrelated conditions. Amongst the treated group (*Table XII*), only one 'tumour death' has been recorded during the period 1953–73. This appears to have resulted from both extensive local infiltration at presentation and inadequacies in the treatment prescribed. Primary treatment, following confirmatory lymph node biopsy, was achieved with external irradiation alone. Thyroxine was not introduced until 10 months later following the development of systemic metastases. Thyroidectomy was not performed. Only one other patient has shown evidence of spread from papillary carcinoma. In this patient local infiltration made total excision impossible. She has therefore been treated with radioactive iodine.

In the remaining patients, tumours were confirmed within the thyroid capsule. Unilateral or bilateral resections were performed in response to operative findings. In no case was thyroid resection extended at a second operation in response to the histological findings. Histological examinations were always performed on 'representative sections'.

Follicular: Ten follicular carcinomas were treated during 1953–73. One other case was noted incidentally at post-mortem.

Three patients died from disseminated carcinoma, while a fourth died with a hemiplegia 2 weeks following operation (*Table XIII*). The 3 'tumour deaths' occurred in patients who presented with locally invasive carcinoma. Complete surgical excision was not possible and therefore radical radiotherapy was employed. Despite the resultant thyroid destruction, 2 patients never received thyroxine, while in the third (M. S., 1967) it was given only after the development of frank myxoedema. Clearly these hormone-dependent tumours were exposed to high levels of thyroid-stimulating hormone.

Two patients went on to develop metastatic carcinoma which has since been controlled. In both, carcinoma had extended locally and was eradicated by combined surgery and radiotherapy. Thyroxine was prescribed for one of these (J. J., 1958) only after the development of myxoedema. This patient had had a previous thyroidectomy for non-toxic multinodular goitre. The second patient (P. G., 1966) required tracheostomy for tracheal collapse 1 year after thyroidectomy. Locally invasive carcinoma was then discovered.

Only 4 patients remain recurrence-free. In these, carcinoma was confined within the thyroid capsule, facilitating complete excision. Clearly only one of this group (L. R., 1957) has been followed for any length of time, but it is significant that no patient with disseminated growth had tumour confined to the thyroid when first seen.

Anaplastic: Thirteen patients were treated for anaplastic carcinoma, while 4 others with advanced disease died rapidly with no treatment. With 3 exceptions, all the patients died within 5 months of presentation. Extensive local infiltration was a feature in all the cases. Seventy-five per cent of the patients developed systemic metastases.

Of the 3 patients who survived for longer than 5 months, one has since died at 3 years. This patient's carcinoma was atypical in exhibiting areas of both 'trabecular and follicular' pattern. The other 2 patients are alive with recurrent disease at 15 and 20 months. The latter has a 'fibrosarcomatous' tumour similar to those described by Woolner et al. (1961).

Mixed follicular-papillary: Only 6 tumours of this kind were recorded and one of these was noted incidentally at post-mortem. Four patients have remained recurrence free (average follow-up 8 years) following unilateral or bilateral subtotal thyroidectomy. Two of these, showing evidence of microscopic invasion, were in addition treated with external irradiation and thyroxine. The fifth developed local neck recurrence and deposits in her thyroidectomy scar. These have responded well to repeat surgery, radioactive iodine and suppressive doses of thyroxine. She is recurrence-free at 11 years.

Discussion

Carcinoma of the thyroid can present in several forms and it is certainly true to say that 'any goitre may be malignant' (Staunton and Greening, 1973). A percentage of these will be clinically apparent although estimates range between 10 per cent (Hurxthal and Heinemann, 1958) and 66 per cent (Till, 1965). It would appear that in specialized centres a preoperative diagnosis should be achieved in 50–60 per cent of all cases (Beahrs et al., 1951; Alhadeff et al., 1956; Shimaoka et al., 1962). The figure of 38·9 per cent reported in this series represents that of a non-specialist district general hospital.

Of great concern is the group of patients whose carcinoma presents in a form often indistinguishable from that of benign goitres; 61·1 per cent of patients in this series fall within this category. The recommendation of Shimaoka et al. (1962) that goitres should be classified as 'benign', 'cancer suspected' and 'cancer probable' would seem to be of value. In attempting to differentiate thyroid cancer from

Table XII: DETAILS OF PATIENTS TREATED FOR PAPILLARY CARCINOMA

				Treatment		
Patient	Age	Sex	Stage of carcinoma at presentation	Surgery	Radiotherapy, hormonal	Follow-up
C. H., 1956	25	F	Confined to thyroid	Bilateral subtotal thyroidectomy	Nil	Recurrence-free at 15 yr
G. J., 1959	70	M	Extensive local infiltration	Lymph node biopsy	External irradiation (thyroxine)	Death from tumour at 2 yr
M. M., 1960	31	F	Confined to thyroid	Bilateral subtotal thyroidectomy	Nil	Recurrence-free at 14 yr
A. P., 1962	41	F	Confined to thyroid	Bilateral subtotal thyroidectomy	^{131}I thyroxine	Recurrence-free at 12 yr
R. S., 1964	41	F	Confined to thyroid	Right subtotal lobectomy	Nil	Recurrence-free at 7 yr
M. B., 1969	34	F	Confined to thyroid	Right subtotal lobectomy	Nil	Recurrence-free at 1 yr Emigrated.
J. A., 1973	26	F	Confined to thyroid	Resection of isthmus	Nil	Recurrence-free at 1 yr
M. F., 1973	79	F	Local infiltration	Right subtotal lobectomy. Incomplete excision	^{131}I	Follow-up 3 mth

Table XIII: DETAILS OF PATIENTS TREATED FOR FOLLICULAR CARCINOMA

				Treatment		
Patient	Age	Sex	Stage of carcinoma at presentation	Surgery	Radiotherapy, hormonal	Follow-up
G. P., 1953	44	M	Extensive local infiltration	Left partial lobectomy. Incomplete removal	External irradiation	Death from tumour at 9 yr
L. R., 1957	58	F	Confined to thyroid	Local excision	Nil	Recurrence-free at 16 yr
J. J., 1958	34	F	Local infiltration	Bilateral subtotal thyroidectomy	External irradiation (thyroxine)	Bone secondary at 13 yr; treated with radiotherapy. Recurrence-free at 16 yr
P. B., 1965	88	F	Presented with scalp secondary	Lymph node biopsy	External irradiation. ^{131}I	Death from tumour at 2 yr
P. G., 1966	44	F	Local infiltration	Bilateral subtotal thyroidectomy. Tracheostomy	External irradiation. ^{131}I. Thyroxine	Bone secondary at 4 yr, lung 5 yr; treated with external irradiation. No active disease at 7 yr
M. S., 1967	86	F	Local infiltration	Bilateral subtotal thyroidectomy. Incomplete resection. Tracheostomy	External irradiation. ^{131}I. Thyroxine	Death from tumour at 3 yr
C. W., 1968	35	F	Confined to thyroid	Right subtotal lobectomy	Nil	Recurrence-free at 5 yr
G. E., 1971	86	M	Confined to thyroid	Bilateral subtotal thyroidectomy	Nil	Recurrence-free at 3 yr
B. B., 1972	34	M	Confined to thyroid	Right subtotal thyroidectomy	Nil	Recurrence-free at 1½ yr
D. I., 1973	47	F	Extensive local infiltration	Incomplete excision. Tracheostomy	Nil	Postoperative death

benign goitre they achieved a high degree of correlation between actual and suspected cancer incidences.

When it was not possible to arrive at a histological diagnosis on purely clinical grounds the patients in this series were categorized as shown in *Table IV*. They were observed to have either a solitary nodule or generalized goitre, which was invariably non-toxic. The difference in behaviour of solitary nodule carcinomas and those presenting as multinodular goitre seems to suggest that they represent stages in a continuous process (*Table VII*). Cases not diagnosed at the solitary nodule stage may present later with a multinodular form.

It is well recognized that from 61·7 per cent (Rose et al., 1963) to 80 per cent (Clark et al., 1966) of unilateral thyroid cancers have demonstrable intraglandular dissemination. These microscopic foci may explain the transformation of a malignant solitary nodule into the multinodular form. Cases presenting at a more advanced stage are invariably diagnosed as carcinoma. This scheme applies to differentiated carcinomas only. The rapid progress of anaplastic tumours precludes the recognition of discernible stages. Occasionally a thyroid carcinoma may develop *de novo* in a pre-existing goitre (Burn and Taylor, 1962).

Solitary nodule carcinomas present on average 12 years before those in multinodular goitres. In this series they had been present for a mean of 23 months compared with the 6 years and 8 months of multinodular goitres. In addition, while multinodular carcinomas exhibit significant local and distant metastases, this is rare for solitary nodule carcinoma. The more advanced state of the multinodular carcinoma is reflected in its poorer prognosis. Thus, of 18 patients treated in this category, 6 have died while 4 others are alive with metastases. The survival figures shown in *Table VII* do not indicate the high incidence of metastases occurring in the patients. All the solitary nodule carcinomas responded well to treatment. Clearly it is important to recognize thyroid carcinoma during its solitary nodule phase, when cure may reasonably be attained.

Crile (in Discussion, Crile and Dempsey, 1949) suggested that a 'high index of suspicion' should be directed at all solitary nodules and was able to report a 90 per cent success rate in diagnosing carcinoma preoperatively in solitary nodules. In contrast, Hoffmann et al. (1972) stated that 'there is no way of differentiating benign from malignant solitary nodules and therefore all must be resected'; a view previously expressed by Liechty et al. (1965) and Taylor (1969b).

It is known that only 50 per cent of clinically solitary nodules are truly solitary (Taylor, 1969b). In these, cancer incidences reaching as high as 33 per cent have been recorded (Cattell and Colcock, 1953). The 2·7 per cent incidence reported in this series is lower than that of most other series as it relates to clinically solitary nodules only. This represents the cancer risk amongst patients subjected to thyroidectomy. The vast majority of operations for solitary nodules are therefore performed for benign nodules. Excellent results for solitary nodule carcinoma can only be achieved, however, if the surgery employed prophylactically is at the same time therapeutic for cancer (Crile, 1953). Prophylactic surgery is of no value if it results in local dissemination of incompletely removed carcinoma. Enucleation of solitary nodules as advocated by Lahey and Hare (1951) is clearly inadequate. Taylor (1965) and Shands and Gatling (1970) have recommended total lobectomy as the minimum procedure for solitary nodules.

Hinton and Lord (1945) and Beahrs et al. (1951) advocated the removal of all non-toxic multinodular goitres because of the high incidence of unsuspected carcinoma. The present study confirms this in reporting a 12·8 per cent incidence of carcinoma in non-toxic multinodular goitres. This figure, however, applies to surgical practice only. The incidence of carcinoma in non-toxic multinodular goitre amongst the general population is much lower than that seen surgically. Carcinoma incidences of 10 per cent (Cope et al., 1949), 10·9 per cent (Crile and Dempsey, 1949) and 17·1 per cent (Cole et al., 1949) have previously been reported in excised non-toxic multinodular goitres.

A major problem is the identification of the patients with non-toxic multinodular goitre who require thyroidectomy. Criteria helping to distinguish benign from malignant non-toxic multinodular goitres have been defined (Hurxthal and Heinemann, 1958; Sokal, 1959) in the belief that the removal of all goitres would result in more life lost than saved. Crile (1953) has stated that 'a woman with multinodular goitre would probably be better protected against the development of fatal cancer by removal of a normal appearing breast or cervix than by removal of the goitre'. While this may apply to the population at large, its relevance to the selected patients seen in surgical clinics is less clear. In this situation the processes of selection favouring cancer have a concentrating effect which may be as high as tenfold (Sokal, 1954; Veith et al., 1964). A decision not to operate on a non-toxic multinodular goitre can only be made in the knowledge that carcinoma has not been absolutely excluded. Patients seen in surgical clinics with non-toxic multinodular goitre should therefore be regarded as having selected themselves for surgery.

If total lobectomy is regarded as the minimal surgical procedure for the solitary nodule, then, it has been argued, total thyroidectomy must be the prophylaxis for multinodular goitre (Cope et al., 1949). Lesser procedures may in theory have resulted in local dissemination of carcinoma in 12·8 per cent of the patients seen in this series. Nevertheless, it would be irrational to advise total thyroidectomy, with its attendant complications, in all non-toxic multinodular goitres. A more realistic approach is the employment of bilateral subtotal thyroidectomy, with conversion to total thyroidectomy as needed. McKenzie (1971) has shown that total thyroidectomy eliminates the local recurrences seen to follow less radical operations. It has the added advantage of facilitating treatment with radio-iodine and prevents the transformation of differentiated into anaplastic carcinomas (Clark et al., 1966). In this series total thyroidectomy was not employed in the treatment of differentiated carcinomas and must, in part, be responsible for poor results obtained in the multinodular carcinomas. Wade (1969) has stressed the need to prevent local recurrence in the treatment of differentiated thyroid carcinoma.

Four tumour deaths were recorded amongst the differentiated thyroid carcinomas. All received external irradiation for locally invasive disease. In the single papillary carcinoma thyroxine was not introduced until systemic metastases appeared. Only 1 of the 3 follicular carcinomas received thyroxine and then only after the development of myxoedema. These tumours were clearly exposed to high levels of thyroid-stimulating hormone at a time when suppressive doses of thyroxine should have been employed. The hormonal dependency of differentiated thyroid cancer is now firmly established (Balme, 1954; Crile, 1966) following Dunhill's (1937) initial observation of tumour regression when treated with thyroid extract. It is imperative, therefore, that when dealing with differentiated thyroid carcinoma periods of hypothyroidism should be restricted to a minimum. This applies equally to carcinoma undergoing treatment with radioactive iodine (Crile and Wilson, 1959). A clearer understanding of the value of thyroxine, coupled with a wider use of total thyroidectomy, would have undoubtedly improved the prognosis amongst the patients reported in this series.

The prognosis of any cancer is determined primarily by its histological type and clinical stage. Good results obtained in treating differentiated thyroid carcinoma compare markedly with those obtained with anaplastic growths. While confirming this, the present study emphasizes the importance of clinical staging of the primary tumour. Clinically obvious carcinomas carry uniformly bad prognoses. They are invariably anaplastic as differentiated carcinomas reach this stage far less frequently. The slower growth of differentiated cancer usually results in them presenting at an earlier stage, when they may be mistaken for benign goitres. Differences in the pattern of behaviour of differentiated carcinomas at these early stages suggest that they pass through solitary nodule and multinodular forms before presenting the picture of a frankly malignant locally invasive goitre. These results emphasize the value of TNM staging when applied to thyroid cancer (Harmer, 1969). Fujimori (1969) was able to relate prognosis to the individual components of the TNM classification and clearly showed that increasing 'T number' was accompanied by worsening of prognosis.

Acknowledgements

We wish to thank Mr J. McKinnell, Consultant Pathologist, for reviewing the histological preparations and confirming diagnoses for all our patients.

Our thanks are also due to Miss J. Powell of the Regional Cancer Registry for her invaluable help, particularly in the preparation of data referable to the Birmingham region.

References

ALHADEFF R., SCOTT F. and TAYLOR S. (1956) A clinicopathological study of thyroid carcinoma. *Br. J. Surg.* **43**, 617–626.

BALME H. (1954) Metastatic carcinoma of the thyroid successfully treated with thyroxine. *Lancet* **1**, 812–813.

BEAHRS O. H., PEMBERTON J. and BLACK B. M. (1951) Nodular goiter and malignant lesions of the thyroid gland. *J. Clin. Endocrinol. Metab.* **11**, 1157–1165.

BURN J. I. and TAYLOR S. F. (1962) Natural history of thyroid carcinoma. *Br. Med. J.* **2**, 1218–1223.

CATTELL R. B. and COLCOCK B. P. (1953) The present day problem of cancer of the thyroid. *J. Clin. Endocrinol. Metab.* **13**, 1408–1415.

CLARK R. L., IBANEZ M. L. and WHITE E. C. (1966) What constitutes an adequate operation for carcinoma of the thyroid? *Arch. Surg.* **92**, 23–26.

COLE W. H., MAJARAKIS J. D. and SLAUGHTER D. P. (1949) Incidence of carcinoma of the thyroid in nodular goiter. *J. Clin. Endocrinol. Metab.* **9**, 1007–1011.

COPE O., DOBYNS B. M., HAMLIN E. and HOPKIRK J. (1949) What thyroid nodules are to be feared? *J. Clin. Endocrinol. Metab.* **9**, 1012–1022.

CRILE G. (1953) Adenoma and carcinoma of the thyroid gland. *New Engl. J. Med.* **249**, 585–590.

CRILE G. (1966) Endocrine dependency of papillary carcinoma of the thyroid. *JAMA* **195**, 721–724.

CRILE G. (1971) Changing end results in patients with papillary carcinoma of the thyroid. *Surg. Gynecol. Obstet.* **132**, 460–488.

CRILE G. and DEMPSEY W. S. (1949) Indications for removal of non-toxic nodular goiter. *JAMA* **139**, 1247–1250.

CRILE G. and WILSON D. H. (1959) Transformation of a low grade papillary carcinoma of the thyroid to an anaplastic carcinoma after treatment with radioiodine. *Surg. Gynecol. Obstet.* **108**, 357–360.

CUELLO C., CORREA P. and EISENBERG H. (1969) Geographic pathology of thyroid carcinoma. *Cancer* **23**, 230–239.

DONIACH I. (1969) Epidemiology of thyroid cancer. *J. R. Coll. Surg. Edinb.* **14**, 261–262.

DUNHILL T. P. (1937) The surgery of the thyroid gland. *Trans. Med. Soc. Lond.* **60**, 234–282.

FUJIMORI M. (1969) Clinical classification of thyroid carcinoma in Japan by T.N.M. system. In: HEDINGER C. E. (ed.) *Thyroid Cancer.* UICC Monograph Series, vol. 12. London, Heinemann, pp. 249–251.

HARMER M. H. (1969) Application of the T.N.M. classification rules to malignant tumours of the thyroid gland. In: HEDINGER C. E. (ed.) *Thyroid Cancer* UICC Monograph Series, vol. 12. London, Heinemann, pp. 246–247.

HINTON J. W. and LORD J. W. (1945) Is surgery indicated in all cases of nodular goiter? *JAMA* **129**, 605–606.

HOFFMANN G. L., THOMPSON N. W. and HEFFRON C. (1972) The solitary thyroid nodule. *Arch. Surg.* **105**, 379–385.

HURXTHAL L. M. and HEINEMANN A. C. (1958) Nodular goiter and thyroid cancer. *New Engl. J. Med.* **258**, 457–465.

JACOBS H. S. and LAWTON N. F. (1974) Pituitary and placental glycopeptide hormones. *Br. Med. Bull.* **30**, 55–61.

LAHEY F. H. and HARE H. F. (1951) Malignancy in adenomas of the thyroid. *JAMA* **145**, 689–695.

LIECHTY R. D., GRAHAM H. and FREEMEYER P. (1965) Benign solitary thyroid nodules. *Surg. Gynecol. Obstet.* **121**, 571–573.

MCKENZIE A. D. (1971) The natural history of thyroid cancer. *Arch. Surg.* **102**, 274–277.

MEISSNER W. A. and WARREN S. (1969) Tumors of the thyroid gland. In: *Atlas of Tumor Pathology*, 2nd ser., fascicle 4. Washington, Armed Forces Institute of Pathology.

OLEN E. and KLINCK G. H. (1966) Hyperthyroidism and thyroid cancer. *Arch. Pathol.* **81**, 531–535.

ROSE R. G., KELSEY M. P., RUSSELL W. O., IBANEZ M. L., WHITE E. L. and CLARK R. L. (1963) Follow up study of thyroid cancer treated by unilateral lobectomy. *Am. J. Surg.* **106**, 494–500.

SHANDS W. C. and GATLING R. R. (1970) Cancer of the thyroid—review of 109 cases. *Ann. Surg.* **171**, 735–745.

SHIMAOKA K., BADELLO J., SOKAL J. E. and MARCHETTA F. C. (1962) Clinical differentiation between thyroid cancer and benign goiter. *JAMA* **181**, 179–185.

SOKAL J. E. (1954) Incidence of malignancy in toxic and non-toxic nodular goiter. *JAMA* **154**, 1321–1325.

SOKAL J. E. (1959) The problem of malignancy in nodular goiter. *JAMA* **170**, 405–412.

STAUNTON M. D. and GREENING W. P. (1973) Clinical diagnosis of thyroid cancer. *Br. Med. J.* **4**, 532–535.

TAYLOR S. (1965) Surgical treatment of carcinoma of the thyroid. *Br. J. Surg.* **52**, 740–742.

TAYLOR S. (1969a) Carcinoma of the thyroid gland. *J. R. Coll. Surg. Edinb.* **14**, 183–192.

TAYLOR S. (1969b) The solitary thyroid nodule. *J. R. Coll. Surg. Edinb.* **14**, 267–271.

TILL A. S. (1965) Types of carcinoma of the thyroid and their presentation. *Br. J. Surg.* **52**, 734–735.

VEITH F. J., BROOKS J. R., GRIGSBY W. P. and SELENKOW H. A. (1964) The nodular thyroid gland and cancer. *New Engl. J. Med.* **270**, 431–436.

WADE J. S. H. (1969) Review of thyroid carcinomas in the United Cardiff Hospitals. *Proc. R. Soc. Med.* **62**, 812–814.

WATERHOUSE J. A. H. (1974) *Cancer Handbook of Epidemiology and Prognosis*. Edinburgh, Churchill Livingstone, p. 174.

WENLOCK R. W. (1974) Personal communication. Ministry of Agriculture, Fisheries and Food.

WILSON W. W. (1973) Thyroid disease and some complications. *Ann. R. Coll. Surg. Engl.* **53**, 27–39.

WOOLNER L. B., BEAHRS O. H., BLACK B. M., MCCONAHEY W. M. and KEATING F. R. (1961) Classification and prognosis of thyroid carcinoma. *Am. J. Surg.* **102**, 354–387.

the range is ours
the choice is yours

ETHICON
TRADEMARK
Eyeless needled sutures

REDUCE TRAUMA

ETHICON* Eyeless Needled Sutures offer three outstanding advantages over traditional eyed needles.

Point 1 Reduced trauma–with ETHICON eyeless needles there is no large eye and only one strand of material to pass through tissue.

Point 2 Consistent high quality–by precisely controlled manufacture of a complete sterile suture in a single package.

Point 3 A new sharp needle every time.

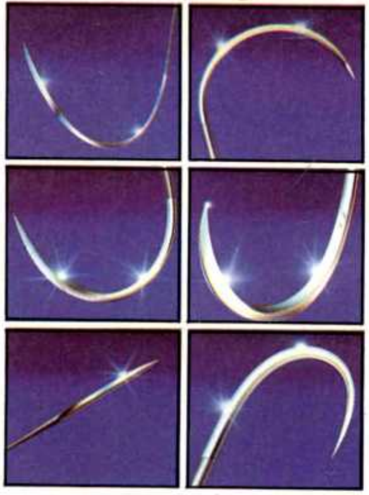
The choice is yours

Most surgeons agree that there is no universal suture. Most probably there never will be. Each patient, each procedure, and each layer of tissue differs from the next. This is why we at ETHICON manufacture such a comprehensive range of eyeless needled sutures.

You can choose from our wide selection of materials, absorbable and non-absorbable, securely attached to a stainless steel needle of your choice. The consistent high quality of ETHICON eyeless needled sutures provides predictable performance. This enables you to concentrate on the most critical aspect of your surgery–the well-being of the patient.

© ETHICON LTD 1974* Trade Mark

Quality and Reliability at every stage



We make some very important points

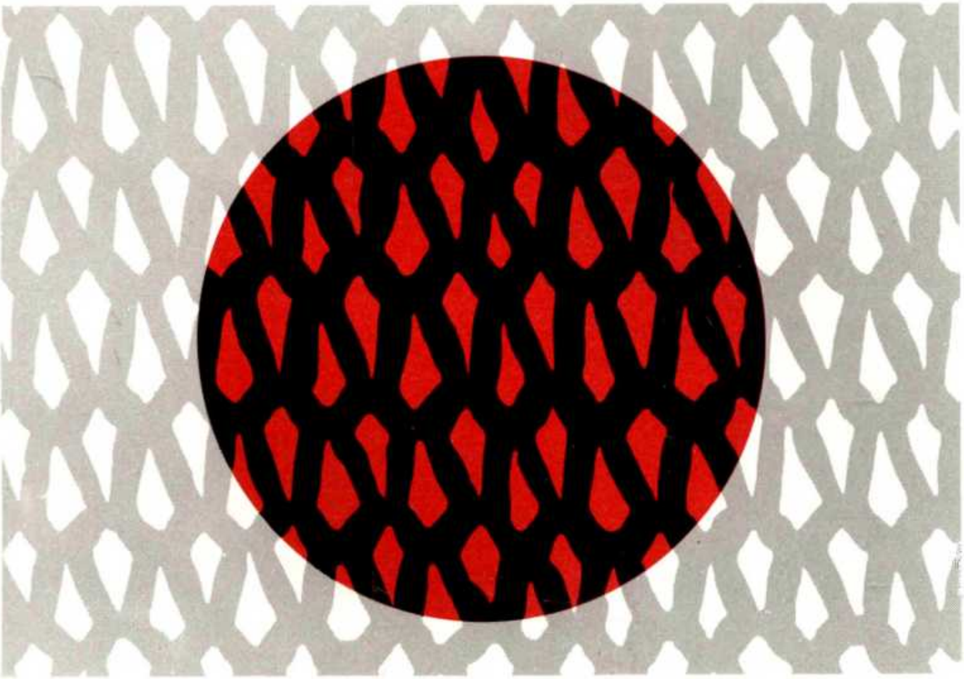
ETHICON
Eyeless needled sutures

Widest range. Finest quality

ETHICON Ltd., Bankhead Avenue, Edinburgh EH11 4HE, Scotland

SURGICEL*

Absorbable Haemostatic Gauze



instantly
controls
bleeding

ETHICON, LTD.

*Trademark ©ETHICON Ltd 1974

Br. J. Surg. Vol. 62

Motility changes in the antrum after proximal gastric vagotomy

MALCOLM KELLY AND TERENCE KENNEDY*

SUMMARY

The normal pattern of resting and post-prandial motor activity in the gastric antrum has been established by observations in 6 dogs. There was a gradual increase in the amplitude of contraction during the first 2 hours after eating; this was maintained for 3 hours and then declined. For the first 45 minutes terminal antral contraction occurred, partially retaining and triturating the gastric contents. After 45 minutes the waves became sequential, symmetrical, increased in vigour and actively pumped food into the duodenum.

Vagotomy modified the mechanism of the antrum in various ways. Truncal and selective vagotomy reduced the work capability to 20 per cent of its normal value when recorded 1 month after operation. In both groups the waves were disorganized.

Proximal gastric vagotomy abolished the braking mechanism and removed the initial inhibitory stimuli to antral motility. Within 1 month of operation the antrum had regained 58 per cent of its normal work capability and the contractions were well organized.

MOTOR denervation of the stomach is followed by a period of gastric paralysis the duration of which is unknown. This leads to gastric retention, distension and vomiting (Oberhelman and Dragstedt, 1955). Because of this difficulty the operation of vagotomy has been accompanied by a drainage procedure. In the case of pyloroplasty the delicate pyloroduodenal mechanism controlling gastric emptying is destroyed and can never be satisfactorily reconstituted; with gastro-enterostomy this region is simply bypassed. Either of these operations in combination with vagotomy converts a delicate storage and pumping mechanism controlled by fine neuro-facilitatory and inhibitory impulses into a denervated bag which empties precipitantly through a large hole in its wall. It is this transformation that produces the undesirable sequelae of dumping and diarrhoea following the operation of vagotomy and drainage.

In 1957 Griffiths and Harkins suggested that gastric stasis could be avoided after vagotomy if the nerves to the antrum were preserved. The production of acid by the stomach would be reduced by dividing the branches supplying the parietal cell mass only. However, the important antral pump would remain intact.

More recently, a number of centres (Amdrup and Jensen, 1970; Johnston and Wilkinson, 1970) have undertaken clinical trials of proximal gastric vagotomy, and follow-up data are accumulating, but there is no precise information about the changes in motility of the antrum after the operation. The present study investigated the motility in the normal animal before and after truncal, selective and proximal gastric vagotomy.

Method of studying gastric motility

Most of the present knowledge of gastro-intestinal motor activity is based on information from intraluminal pressure recording from balloons or open-tipped manometers (Wheelon and Thomas, 1920; Hightower and Code, 1950; Creamer et al., 1956; Harris and Pope, 1964; Edwards, 1965). Both methods are subject to artefacts due to transmitted pressure waves, interference with the flow of alimentary material or obstructed tubing. They are both difficult to locate precisely.

Because of these limitations a miniaturized mercury column strain gauge was developed for this investigation (Kelly et al., 1972). It consists of a fine silicone rubber tube filled with mercury under pressure (*Fig.* 1). As the tubing is stretched the column of mercury becomes longer and narrower, changing its electrical resistance. This in turn produces a signal which is amplified and recorded. Prior to implantation the gauges were calibrated in a waterbath at 37 °C to ensure a linear response over the working range of 4–6 cm.

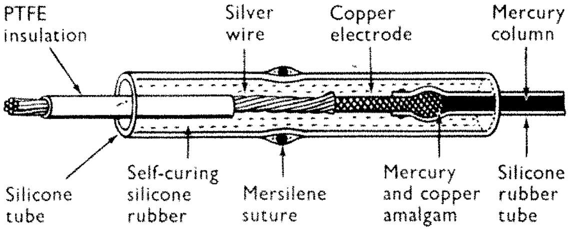


Fig. 1. The mercury strain gauge; transverse section through one end of a gauge showing the junction between the mercury, the wire and the electrode.

An *in vivo* trial was carried out on a small number of gauges to confirm that the response was both linear and meaningful. A latex balloon was placed in the stomach and inflated with CO_2. As the circumference of the antrum increased, the gauge increased in length, producing a corresponding pen deflection; this was compared with the actual measurement of the circumference and found to be directly linear (*Fig.* 2).

---

* Royal Victoria Hospital, Belfast.

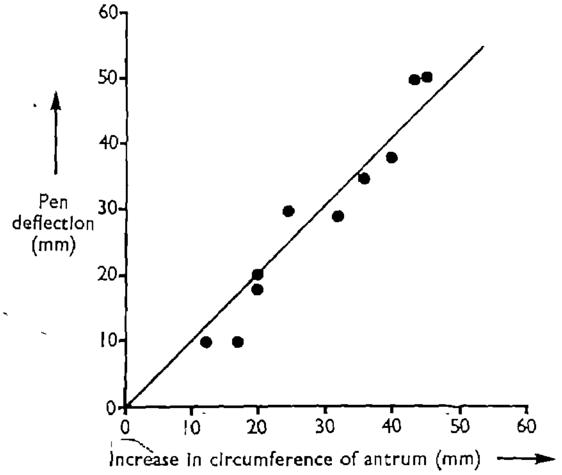


Fig. 2. *In vivo* calibration; graph of the increase in circumference of the antrum plotted against pen deflection on the Devices M19 recorder.

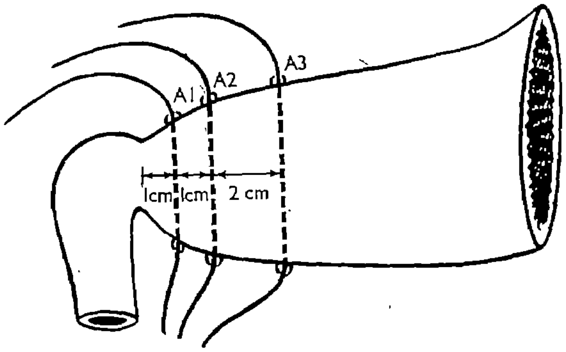


Fig. 3. Pyloric antrum and first part of duodenum showing the position of the gauges.

Implantation was carried out in sterile operating conditions under general anaesthesia. The gauges were accurately positioned on the serosal surface of the stomach at A1 (1 cm), A2 (2 cm) and A3 (4 cm) from the pylorus (*Fig.* 3) and sutured in place. An adequate length of wire was left in the peritoneal cavity; the ends of the wire were taken out through a stab wound in the right flank, and then subcutaneously to the dorsal surface of the neck. Here each wire was threaded on to a needle and brought out through individual puncture holes in the skin of the neck.

Vagotomy was performed at the same time as implantation, where this was appropriate.

Motility index and work capability

Motility recordings were made at weekly intervals after implantation of the gauges. The results at 1 month were used for comparison as they were found to be consistent and repeatable. Recordings made in the early postoperative period usually showed a disorganized pattern of varying amplitude. The dog was given a mixed meat meal and the recordings were continued for a 7-hour post-prandial period. A motility index was obtained from the trace every 15 minutes by measuring the total excursion of gauge A2 in mm over a period of 1 minute. A graph representing the total post-prandial motility was then plotted from these results.

In a number of the experiments the meal was mixed with barium powder and simultaneous radiological screening was performed. This enabled the gastric emptying to be directly related to the motility recording.

By measuring the area under the post-prandial motility graph it was possible to obtain a numerical representation of the amount of work performed by the antrum in the 7-hour period. Although the figure

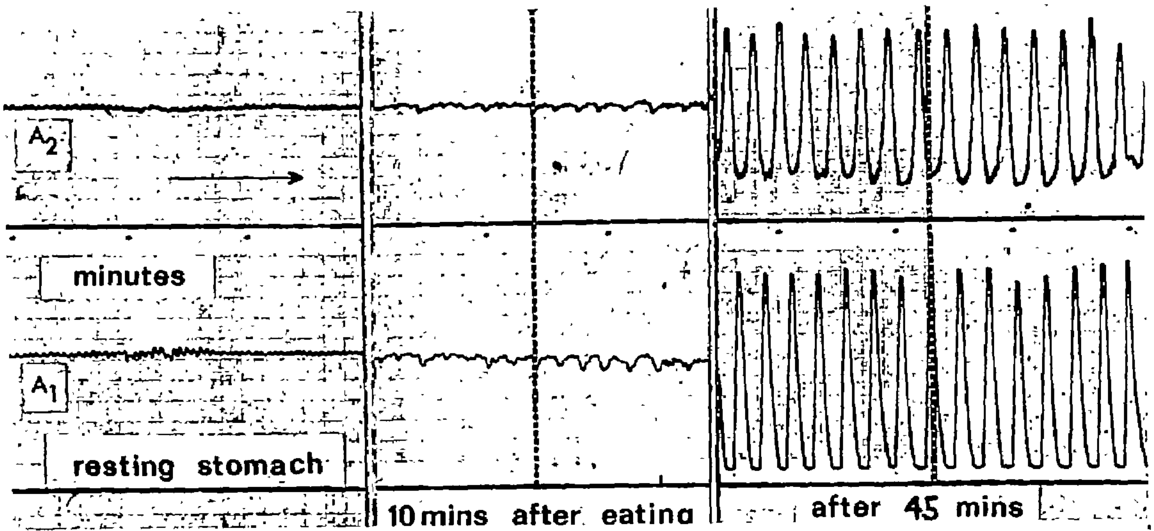


Fig. 4. Composite motility trace showing recordings from the stomach when resting, 10 minutes after eating and 45 minutes after eating. Shortly after eating, contractions at A1 and A2 occur simultaneously. A2 precedes A1 when emptying is well established.

was not an absolute value of work done in foot pounds it was nevertheless useful for comparing the work capability of the stomach after the various types of vagotomy.

Results

The normal stomach

Terminal antral contraction: Shortly after eating it was found that the gauges at A1 and A2 contracted simultaneously (*Fig*. 4), indicating that the terminal antral segment had contracted as a unit. Simultaneous radiological screening studies showed that food was predominantly retained at this time (*Fig*. 5). After 45 minutes the waves at A1 and A2 separated over the course of 5 minutes to become sequential and continued to increase in vigour. During this type of activity simultaneous radiological screening studies showed food being actively pumped into the duodenum.

Post-prandial motility contour: In the normal stomach (*Fig*. 6) there was a gradual build-up of motility for the first 2 hours after eating; this was maintained for 3 hours, then gradually declined. The hatched area under the graph represents the time during which terminal contraction was taking place and food was predominantly retained in the stomach. The dotted area represents sequential peristaltic activity when the food was actively pumped into the duodenum. The total area under the graph was taken as the total work capability of the normal antrum and represents 100 per cent activity.

After vagotomy

Nine dogs were subjected to vagotomy—3 truncal, 3 selective and 3 proximal gastric vagotomies. Strain gauges were implanted at the time of operation. One month later an insulin test was carried out to ensure that the vagotomy was complete, and motility was recorded.

After truncal vagotomy there was a dramatic decrease in overall motility and work capability of the antrum (*Fig*. 7). Not only was the amplitude of contraction diminished but the motility was disorganized. There were long periods of quiescence interspersed with bursts of activity (*Fig*. 8). This was quite unlike the regular high amplitude pattern seen in the normal stomach at this time. The total work capability was 22 per cent of normal. The changes following selective vagotomy were virtually identical (*Fig*. 9), the total work capability being 13 per cent of normal. When these animals were screened after a meal mixed with barium, the liquid part of the meal was seen to leave the stomach immediately, whilst the solid part remained for many hours.

After proximal gastric vagotomy the pattern was different. First, the overall motility was well maintained (*Fig*. 10). A most interesting feature was the speed with which high amplitude contractions occurred (*Fig*. 11). Within 10 minutes of eating they had reached their maximum values. In the normal stomach this was only attained 2 hours after eating. There was no initial period of terminal antral

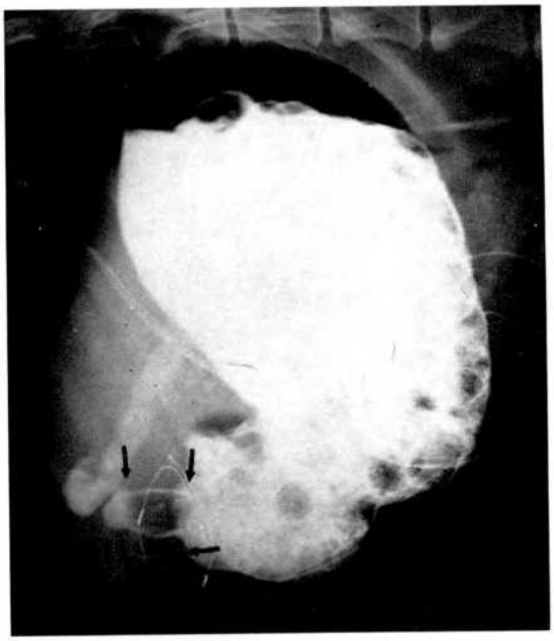


Fig. 5. X-ray film of the dog's stomach with strain gauges A1 and A2 *in situ* taken 10 minutes after eating. The arrows indicate the terminal antral contraction.

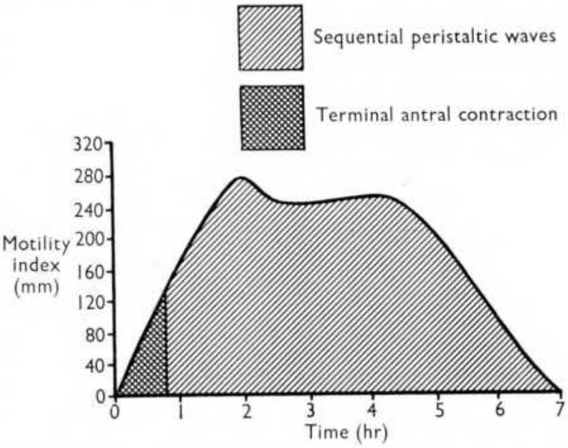


Fig. 6. Average post-prandial motility contour of 6 normal dogs. Area under graph, 240 cm².

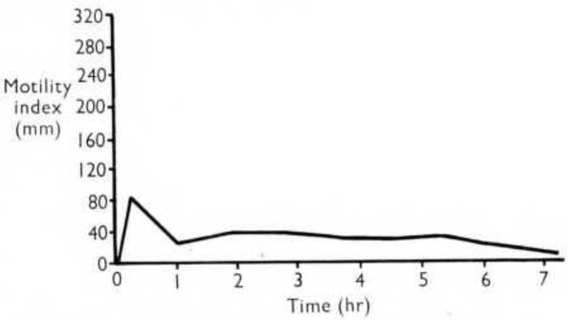


Fig. 7. Average post-prandial motility contour of 3 dogs 1 month after truncal vagotomy. Area under graph, 54 cm².

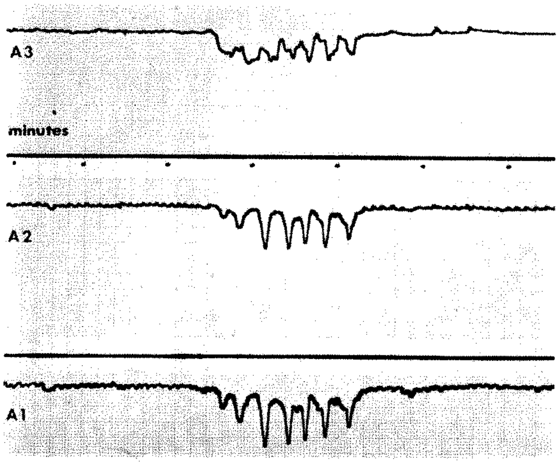


Fig. 8. Motility recordings from A1, A2 and A3 after truncal vagotomy showing augmented burst activity, recorded 2 hours after eating.

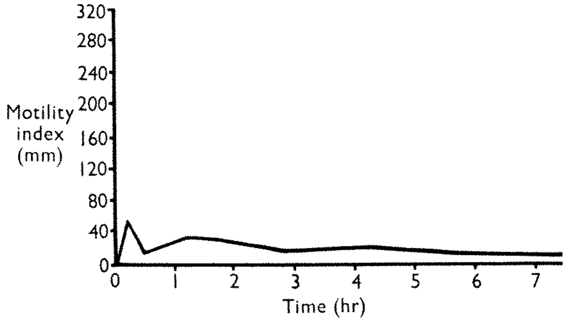


Fig. 9. Average post-prandial motility contour of 3 dogs 1 month after selective vagotomy. Area under graph 31 cm².

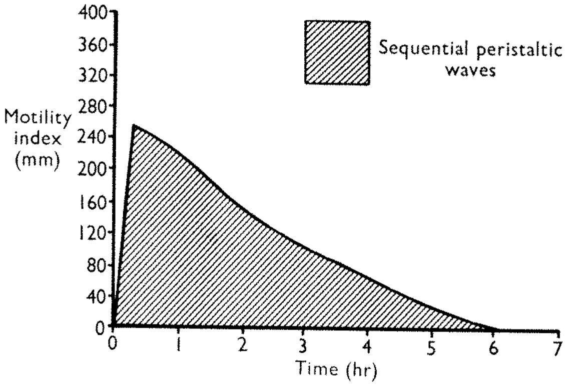


Fig. 10. Average post-prandial motility contour of 3 dogs 1 month after proximal gastric vagotomy. Area under graph 138 cm².

contraction. From the moment food was taken simultaneous radiological screening studies showed sweeping waves pumping it into the duodenum. The total work capability was 58 per cent of normal.

Throughout the period of this study all the dogs in the proximal gastric vagotomy group remained in good health, maintaining or even gaining weight. Following selective or truncal vagotomy the dogs did less well, losing an average of 4·0 kg. Each study was concluded at 6 months and a post-mortem examination was carried out. There was no gross change in the antrum or pyloric ring of the proximal gastric vagotomy group, but in both the selective and the truncal groups the antrum was dilated and saccular, and the circumference of the pyloric ring was consistently greater than in normal dogs.

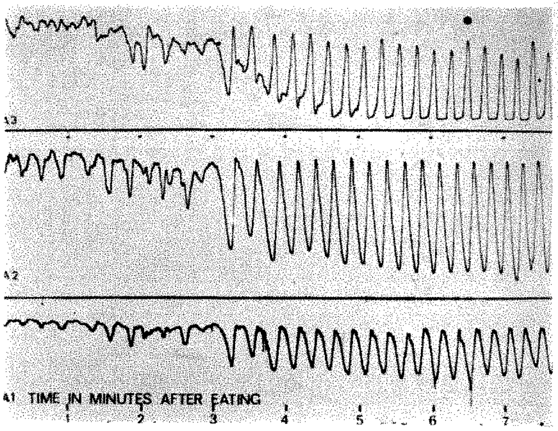


Fig. 11. Motility trace from gauges A1, A2 and A3 recorded 3 weeks after proximal gastric vagotomy. It shows that contractions have reached almost maximum amplitude within 7 minutes of eating.

Discussion

The operation of proximal gastric vagotomy is performed without a drainage operation. It aims to reduce gastric acidity and to allow the duodenal ulcer to heal whilst maintaining antral motility and effective gastric emptying. Does it achieve this? To confirm the effectiveness of vagotomy in this animal study, insulin stimulation tests were performed 1 month postoperatively. These were all negative according to Hollander's criteria. In a pilot study of 20 patients who underwent proximal gastric vagotomy in 1970 in the Royal Victoria Hospital, Belfast, the Hollander test was found to be negative in all the patients when measured on the tenth postoperative day. This was similar to the findings of Johnston and Wilkinson (1970).

The present investigation has shown that the avoidance of a drainage operation in combination with proximal gastric vagotomy maintains an active and effective pyloric pump which recovers rapidly after operation. This was in sharp contrast to the almost complete absence of motor activity seen after truncal and selective vagotomy. Stasis is unlikely to occur after proximal gastric vagotomy.

Without a drainage procedure the pyloric ring remains intact and will completely close at the end of each peristaltic cycle. This was first shown by Hofmeister and Schutz (1886) and by Moritz and Tschr (1901). It was confirmed by Cole (1913) and studied in detail by Quigley and Meschan (1941). The contracted pylorus not only provides a 'breach block' for duodenal contraction, but prevents the regurgitation of bile, a common problem after either pyloroplasty or gastrojejunostomy.

It was Cannon in 1898 who first pointed out that the pyloric region of the stomach had a more important function than that of merely expelling gastric contents into the intestine. He found that adding a hard pellet of starch to a gruel and bismuth meal given to a cat delayed gastric emptying from 15 to 45 minutes. Carlson et al. (1966), using cineradiographic techniques, described the mechanism through which this delay in gastric emptying was brought about. When peristaltic waves reach the antrum they produce a diaphragm which may or may not completely separate the antrum from the body of the stomach. At this moment a contraction involving the whole of the terminal antral segment, including the pyloric sphincter, occurs. Alimentary contents will be forcefully ejected into the duodenum until such time as the pyloric sphincter closes and prevents this flow. Since the pyloric canal is much narrower than the rest of the antrum it remains closed throughout the continuation of the terminal antral contraction. At other times the pyloric canal will narrow early in the cycle but not completely close so that movement of the contents through it into the duodenum occurs while the antrum continues to contract. This agrees with Hunt's (Hunt and Knox, 1968) theory of the regulation of gastric emptying, depending on the timing of the closure of the pylorus, during antral systole.

An unexpected finding in the present study was the complete absence of terminal antral contraction—and the 'antral braking mechanism'—after all types of vagotomy. Following a normal meal there is an initial period during which very little emptying occurs from the dog's stomach. The food is held back by a combination of contractions involving the terminal 3 cm of antrum, high antral tone and low amplitude peristaltic waves. The result of this is retropulsion of food into the body of the stomach. This capability is lost after vagotomy.

After proximal gastric vagotomy high amplitude peristaltic waves occur within minutes of eating, pumping the food into the duodenum with the result that a hypertonic meal could be delivered into the duodenum before equilibration, producing dumping. This finding has been confirmed in man by Clarke and Alexander-Williams (1973). They found that the initial emptying of a fluid meal was faster after proximal gastric vagotomy than in the normal individual. Dumping has been reported in various clinical trials (Humphrey et al., 1972; Clarke and Alexander-Williams, 1973). In our own pilot study 40 per cent of the patients admitted to mild transitory dumping at some time during the early postoperative period, but at 1 year after operation none had significant dumping symptoms.

The study has also thrown light on the phenomenon of dumping after the more conventional truncal and selective vagotomy. Again the braking mechanism was found to be completely absent after operation. Both radiological screening studies and post-mortem findings showed the antrum to be dilated and saccular, and the circumference of the pyloric ring to be consistently greater than in normal animals. It might be said that the denervated stomach behaves like the neurogenic bladder; if allowed to overdistend, as in the case of truncal and selective vagotomy without drainage, it becomes a dilated bag which empties by overflow.

Although the finer mechanisms of the antrum are disorganized after proximal gastric vagotomy, vigorous peristaltic activity remains, emptying is satisfactory and it is therefore unnecessary to perform an accompanying drainage operation.

Acknowledgements

This work was supported by a grant from the Royal Victoria Hospital, Belfast, and was part of a thesis for the Mastership in Surgery of London University in 1973.

References

AMDRUP E. and JENSEN H. E. (1970) Selective vagotomy of the parietal cell mass preserving innervation of the undrained antrum: a preliminary report of results in patients with duodenal ulcer. *Gastroenterology* **59**, 522–527.

CANNON W. B. (1898) Movements of the stomach studied by roentgen rays. *Am. J. Physiol.* **1**, 359.

CARLSON H. C., CODE C. and NELSON R. A. (1966) Motor action of the canine gastroduodenal junction. A cineradiographic pressure and electrical study. *Am. J. Dig. Dis.* **11**, 155–172.

CLARKE R. J. and ALEXANDER-WILLIAMS J. (1973) The effect of preserving antral innervation and of a pyloroplasty on gastric emptying after vagotomy in man. *Gut* **14**, 300–307.

COLE L. G. (1913) Physiology of the pylorus, pilleus ventriculi and duodenum as observed roentgenographically. *JAMA* **61**, 762.

CREAMER B., ANDERSEN H. A. and CODE C. F. (1956) Oesophageal motility in patients with scleroderma and related disease. *Gastroenteroligia* **86**, 763.

EDWARDS D. A. W. (1965) Techniques and interpretations of measurement of gastrointestinal pressures. *Ann. R. Coll. Surg. Engl.* **37**, 275–284.

GRIFFITHS C. A. and HARKINS H. N. (1957) Partial gastric vagotomy—an experimental study. *Gastroenterology* **32**, 96.

HARRIS L. D. and POPE C. E. (1964) "Squeeze" versus resistance: an evaluation of the mechanism of sphincter competence. *J. Clin. Invest.* **43**, 2272–2278.

HIGHTOWER N. C. and CODE C. F. (1950) The quantitative analysis of antral gastric motility records in normal human beings, with a study of the effects of neostigmine. *Proc. Staff Meet. Mayo Clin.* **25**, 697–704.

HOFMEISTER F. and SCHUTZ E. (1886) Ueber Resorption und Assimilation der Nährstoffe. *Arch. Exp. Path. Pharmak.* **20**, 7.

HUMPHREY C. S., WILKINSON A. R. and JOHNSTON D. (1972) The correlation between the rate of gastric emptying and dumping and diarrhoea after truncal, selective, and highly selective vagotomy. *Br. J. Surg.* **59**, 309.

HUNT J. N. and KNOX M. T. (1968) Control of gastric emptying. *Am. J. Dig. Dis.* **13**, 372–375.

JOHNSTON D. and WILKINSON A. R. (1970) Highly selective vagotomy without a drainage procedure in the treatment of duodenal ulcer. *Br. J. Surg.* **57**, 289–296.

KELLY J. M., CONNELL A. M., KENNEDY T. L. and CLARKE E. W. (1972) Application of miniaturized mercury column strain gauges to the study of gastric motility. *Am. J. Dig. Dis.* **17**, 455–462.

MORITZ S. and TSCHR Z. (1901) Ueber die Beziehungen zwischen Arzneien und Magen. *Biol.* **42** (NS 24), 565.

MURRAY J. G. (1969) Regeneration of the vagus nerve. In: ALEXANDER-WILLIAMS J. and COX A. G. (ed.) *After Vagotomy.* London, Butterworths, pp. 77–88.

OBERHELMAN H. A. and DRAGSTEDT L. R. (1955) New physiologic concepts related to the surgical treatment of duodenal ulcer by vagotomy and gastroenterostomy. *Surg. Gynecol. Obstet.* **101**, 194–200.

QUIGLEY J. P. and MESCHAN I. (1941) Inhibition of the pyloric sphincter region by the digestive products of fat. *Am. J. Physiol.* **134**, 803–807.

WHEELON H. and THOMAS J. E. (1920) Observations on the motility of the antrum and the relation of the rhythmic activity of the pyloric sphincter to that of the duodenum. *J. Lab. Clin. Med.* **6**, 124.

Br. J. Surg. Vol. 62 (1975) 221–223

The management of bleeding acute gastric erosions: the role of gastric hypothermia

H. S. HIMAL, W. W. WATSON, C. W. JONES AND L. D. MacLEAN*

SUMMARY

Eighty-eight consecutive patients with bleeding acute gastric erosions were reviewed with the aid of a computer. Of the erosions, 31·8 per cent were related to the ingestion of ulcerogenic drugs and 40·9 per cent were associated with surgery and sepsis. The overall mortality was 20·5 per cent. Endoscopy was the most effective diagnostic examination. Conservative management was effective in the treatment of bleeding erosions due to the ingestion of ulcerogenic drugs. Gastric cooling successfully arrested haemorrhage from bleeding erosions due to surgery and sepsis.

Massive haemorrhage from acute ulcerations of the upper gastro-intestinal tract is a formidable problem to manage. Most publications in the literature report a mortality of over 40 per cent (Capper and Buckler, 1964; Lulu and Dragstedt, 1970; David et al., 1971). Although first described early in the nineteenth century (Swan, 1823), Curling (1842) drew attention to the association between burns and acute gastroduodenal ulceration. Subsequent reports have emphasized the relationship between stress ulcers and surgery (Delaney, 1962; Fogelman and Garvey, 1966; Flowers et al., 1970), sepsis (Garvey and Fogelman, 1966; Rosoff and Goldman, 1968; Altemeier et al., 1972; Robbins et al., 1972) and chronic debilitating illness (Katz, 1959; Spencer et al., 1959, Fogelman and Garvey, 1966; Skillman et al., 1969).

A retrospective study of all forms of upper gastro-intestinal bleeding was undertaken by the authors to determine which factors were most commonly associated with mortality (Himal et al., 1974). The overall mortality was 12·54 per cent. The mortality rate correlated with the admission haemoglobin, the amount of blood administered, age and whether the preoperative diagnosis was known.

The present study was undertaken to analyse further, bleeding acute gastric erosions with respect to aetiology, efficacy of various diagnostic procedures and which of the management protocols was associated with the lowest mortality. The clinical impression that drug-induced, in contrast to sepsis-related, acute gastric erosions are associated with minimal mortality was also investigated. The effect of gastric cooling in the management of acute erosions was also assessed.

Materials and methods

Of 630 patients with upper gastro-intestinal haemorrhage seen between 1963 and 1971, 88 cases of bleeding acute gastric erosions were analysed. Each patient's chart was reviewed by one of the authors and the information collected was recorded on a standard data sheet as a 68-character line. This was transcribed via remote access terminal to a central processing and storage unit (IBM 360–75). Each character referenced a line of vocabulary according to its position. The data were processed using conventional set theory in Fortran IVG language. Analysis was carried out with respect to cause of erosions, accuracy of diagnosis and therapy.

Table I: CAUSES OF ACUTE GASTRIC EROSIONS

Initial insult	No. of patients	Mortality No.	Mortality %
Ulcerogenic drugs	28	1	3·6
Surgery and sepsis	36	11	30·5
Debilitating illness	10	4	40·0
Trauma	6	1	16·6
Unknown	8	1	12·6
Total	88	18	20·5

Table II: ACCURACY OF DIAGNOSTIC PROCEDURES

Procedure	No. of patients	Diagnostic accuracy No.	Diagnostic accuracy %
X-rays of the upper gastro-intestinal tract	30	5	16·6
Gastroscopy	50	47	94·0

Results

Causes of acute erosions

Of the 88 patients with bleeding acute erosions, 28 were caused by the ingestion of ulcerogenic drugs (acetylsalicylic acid, ethanol) and 36 were associated with surgery—neurosurgery, gastro-intestinal and cardiac surgery (*Table I*). Sepsis following gastro-intestinal surgery was an important factor. Ten patients had debilitating illness—hepatitis, multiple sclerosis and chronic renal failure. In 6 patients skeletal, spinal cord and blunt abdominal trauma were the predisposing factors. The overall mortality was 20·5 per cent.

Diagnostic procedures

Endoscopic examination of the stomach was the most accurate method of diagnosing bleeding gastric erosions (*Table II*). The accuracy rate was 94 per cent. Of 30 patients who had X-rays of the upper gastro-intestinal tract, in only 5 was there a suggestion of acute gastric erosions (16·6 per cent). At surgery in 12 patients and at post-mortem analysis in 6 patients

---

* Department of Surgery, Royal Victoria Hospital, and McGill University, Montreal, Canada.

Table III: RESULTS OF DIFFERENT FORMS OF THERAPY

Therapy	No. of patients	Success in arresting haemorrhage No.	Success in arresting haemorrhage %	Mortality No.	Mortality %
Conservative	51	39	76·4	8	15·7
Surgery	11	9	81·8	6	54·5
Gastric cooling	26	22	84·6	4	15·3

Table IV: EFFECT OF THERAPY IN ARRESTING HAEMORRHAGE IN DIFFERENT SUBGROUPS OF ACUTE GASTRIC EROSIONS

Initial insult	No. of patients	Therapy	No. of patients	Cessation of haemorrhage
Ulcerogenic drugs	28	Conservative	23	23
		Surgery	3	2
		Gastric cooling	2	2
Surgery and sepsis	36	Conservative	17	9
		Surgery	—	—
		Gastric cooling	19	16
Debilitating illness	10	Conservative	6	3
		Surgery	2	1
		Gastric cooling	2	2
Trauma	6	Conservative	2	2
		Surgery	1	0
		Gastric cooling	3	3
Unknown	8	Conservative	3	3
		Surgery	5	4
		Gastric cooling	—	—

examination revealed bleeding erosions. In 20 patients the only diagnostic assessment was clinical impression.

Management

All the patients had a short course of gastric saline lavage and intravenous therapy for resuscitation or maintenance while the initial diagnostic assessment was being made. Three different forms of therapy were used in this series.

1. *Conservative management*: Oral antacid therapy.
2. *Surgical management*: Operative intervention was the primary treatment.
3. *Gastric cooling*: This therapeutic approach was used only after an initial period of conservative management had failed to arrest the haemorrhage. A gastric balloon was placed per os into the stomach and gastric cooling by the Swenko* cooling machine was performed for 48 hours.

The overall distribution of therapy is displayed in *Table III*. The majority of patients (51) received only conservative therapy, with cessation of bleeding in 39 (76·4 per cent). Eight patients eventually died of their primary disease—malignancy, renal failure. Of 11 patients who had immediate surgery, 9 stopped bleeding. Six, however, died in the postoperative period of anastomotic disruption and localized sepsis. Of 26 patients who had gastric cooling, 22 stopped bleeding. The other 4 patients continued to bleed and therefore underwent surgery, but died of sepsis and haemorrhage.

The various treatment regimens in the different groups of patients are shown in *Table IV*. In patients with haemorrhage due to ulcerogenic drugs, all three forms of therapy were successful in stopping the bleeding. Gastric cooling was successful in patients with post-surgical or sepsis-related bleeding gastric erosions.

Discussion

Bleeding acute gastric erosions or gastritis have now become a prominent cause of upper gastro-intestinal haemorrhage (Foster et al., 1965; Garvey and Fogelman, 1966). Most reports indicate a greater than 30 per cent mortality from either continuous haemorrhage or postoperative complications (Fogelman and Garvey, 1966; Lulu and Dragstedt, 1970; David et al., 1971). The overall mortality in the present study was 20·5 per cent.

This study demonstrated that most bleeding acute gastric erosions (73 per cent) were related to the ingestion of ulcerogenic drugs, surgery and sepsis following surgery. Aspirin and ethanol alter the functional gastric mucosal barrier, increasing the net H^+Na^+ ionic flux, causing mucosal erosions and haemorrhage (Davenport, 1965, 1967). Localized and generalized sepsis can lead to thrombocytopenia, prolongation of the prothrombin time and an increase in gastric acid secretion (Rosoff and Goldman, 1968; David et al., 1971; Altemeier et al., 1972).

X-rays of the upper gastro-intestinal tract, when performed, suggested bleeding acute gastric erosions in only 16·6 per cent of the patients. Because of the shallow aspect of gastric erosions, contrast material frequently does not outline the mucosal defect.

Early endoscopy as the main diagnostic procedure for bleeding acute gastric erosions has previously been emphasized (Katz et al., 1964; Smith and Katon, 1973). In the present report endoscopy, when performed, demonstrated bleeding gastric erosions in 94 per cent of the patients.

Conservative management was most effective in the treatment of bleeding gastric erosions due to ulcerogenic drugs. In all 23 patients the haemorrhage stopped within 6 hours after initiation of antacid therapy.

Gastric erosions associated with surgery and sepsis was a difficult management problem. Conservative treatment led to cessation of haemorrhage in only 9 of 17 patients (53 per cent). Our preliminary experience with surgical treatment of these erosions led to a prohibitive mortality. The literature demonstrates a variable mortality. Flowers et al. (1970) in their series had a 23 per cent mortality, while Girvan and Passi (1971) had a 65 per cent survival rate.

Garvey and Fogelman (1966) reported a 66·7 per cent mortality with surgery. David et al. (1971) showed a greater than 30 per cent mortality with surgical management. Preliminary experience with gastric cooling indicated that this might be an effective therapeutic approach. Gastric hypothermia decreases blood flow through the stomach and duodenum as well as gastric acid secretion (Wangensteen et al., 1959; Peter et al., 1963). Decreased acid bathing the area and decreased blood flow would then favour healing of acute gastric erosions. Gastric cooling was employed in 26 patients and stopped the bleeding in 22 (84·6 per cent). Cooling was particularly effective in erosions associated with surgery and sepsis; the success rate was 84 per cent.

---

* Swenko Gastric Hypothermia Machine, Swenko Research & Development Inc., Minneapolis, Minnesota.

This study suggests that bleeding acute gastric erosions associated with ingestion of ulcerogenic drugs are effectively managed conservatively. Gastric cooling is effective in the management of erosions related to surgery and sepsis. Surgery has little if any role to play in the treatment of acute gastric erosions. Recent studies indicate that intra-arterial infusion of Pitressin may also be effective in the management of bleeding acute gastric erosions (Atharasoulis et al., 1974).

References

ALTEMEIER W. A., FULLEN W. D. and MCDONOUGH J. J. (1972) Sepsis and gastrointestinal bleeding. *Ann. Surg.* **175**, 759–770.

ATHARASOULIS C. A., BAUM S. and WALTMAN A. C. (1974) Intra-arterial posterior extract for acute gastric mucosal hemorrhage. *New Engl. J. Med.* **290**, 597–604.

CAPPER W. M. and BUCKLER K. G. (1964) Determination of the cause of bleeding in surgery for massive haematemesis. *Br. J. Surg.* **51**, 752–754.

CURLING T. B. (1842) An acute ulceration of the duodenum in cases of burn. *Trans. R. Med. Chir.* (Lond.) **25**, 260–261.

DAVENPORT H. W. (1965) Damage to the gastric mucosa: effects of salicylates and stimulation. *Gastroenterology* **49**, 189–196.

DAVENPORT H. W. (1967) Ethanol damage to canine oxyntic glandular mucosa. *Proc. Soc. Exp. Biol. Med.* **126**, 657–662.

DAVID E., MCILLRATH D. C. and HIGGINS J. A. (1971) Clinic experience with acute peptic gastrointestinal ulcers. *Mayo Clin. Proc.* **46**, 15–24.

DELANEY J. P. (1962) Post-operative hemorrhagic gastritis. *Surgery* **51**, 185–194.

FLOWERS R. S., KYLE K. and HOERR S. O. (1970) Postoperative hemorrhage from stress ulceration of the stomach and duodenum. *Am. J. Surg.* **119**, 632–636.

FOGELMAN M. J. and GARVEY J. M. (1966) Acute gastroduodenal ulceration incident to surgery and disease. *Am. J. Surg.* **112**, 651–656.

FOSTER J. H., HICKOK D. F. and DUNPHY J. E. (1965) Changing concepts in the surgical treatment of massive gastroduodenal hemorrhage. *Ann. Surg.* **161**, 968–976.

GARVEY J. M. and FOGELMAN M. J. (1966) Septic peptic ulceration. *J. Trauma* **6**, 644–665.

GIRVAN D. and PASSI R. B. (1971) Acute stress ulceration with bleeding or perforation. *Arch. Surg.* **103**, 116–121.

HIMAL H. S., WATSON W. W. and JONES C. W. (1974) The management of upper gastrointestinal hemorrhage: a multiparametric computer analysis. *Ann. Surg.* **179**, 489–493.

KATZ A. M. (1959) Hemorrhagic duodenitis in myocardial infarction. *Ann. Intern. Med.* **51**, 212–218.

KATZ D., DOUVERS P. and WEISBERG H. (1964) Early endoscopic diagnosis of acute upper gastrointestinal hemorrhage. Demonstration of relatively high incidence of erosions as a source of bleeding. *JAMA* **188**, 405–408.

LULU D. J. and DRAGSTEDT II, L. R. (1970) Massive bleeding due to acute hemorrhagic gastritis. *Arch. Surg.* **101**, 550–554.

PETER E. T., NICOLOFF D. N. and BERNSTEIN E. F. (1963) The effect of gastric hypothermia on splanchnic hemodynamics in the dog. *J. Surg. Res.* **3**, 32–35.

ROBBINS R., IDJADI F. and STAHL W. M. (1972) Studies of gastric secretion in stressed patients. *Ann. Surg.* **175**, 555–562.

ROSOFF C. B. and GOLDMAN H. (1968) Effect of the intestinal bacterial flora on acute gastric stress ulceration. *Gastroenterology* **55**, 212–222.

SKILLMAN J. J., BUSHNELL L. S. and GOLDMAN H. (1969) Respiratory failure, hypotension, sepsis and jaundice: a clinical syndrome associated with lethal hemorrhage from acute stress ulceration of the stomach. *Am. J. Surg.* **117**, 523–530.

SMITH F. W. and KATON R. M. (1973) Panendoscopy in the early diagnosis of acute upper gastrointestinal bleeding. *Gastroenterology* **65**, 728–734.

SPENCER J. A., MARLOCK C. G. and SAYRE G. P. (1959) Lesions in upper portion of the gastrointestinal tract associated with intracranial neoplasms. *Gastroenterology* **37**, 20–27.

SWAN J. (1823) Practical observations: case of a severe burn. *Edin. Med. Surg. J.* **19**, 344–345.

WANGENSTEEN O. H., SALMON P. A. and GRIFFEN W. O. (1959) Studies of local gastric cooling as related to peptic ulcer. *Ann. Surg.* **150**, 346–360.

Br. J. Surg. Vol. 62 (1975) 224–225

A case of haemorrhage from volvulus of the gastric fundus

C. METCALFE-GIBSON*

SUMMARY

Volvulus of the stomach is a rare condition and complications are even more uncommon. A case of haemorrhage complicating volvulus of the gastric fundus is presented.

Case report

W. M., a 60-year-old man, was admitted to hospital following a small haematemesis and the passage of a melaena stool. He was mildly shocked on admission, the pulse rate was 120 per minute, blood pressure 90/70 mm Hg and the haemoglobin was 10·3 g per cent. He responded satisfactorily to a 2-pint blood transfusion, and after 36 hours it was apparent that the haemorrhage had ceased.

His past history included a left phrenic nerve crush at the age of 19 for tuberculosis, and a myocardial infarction treated in hospital 4 months prior to the present admission. He did not give a history of indigestion but for 2 months before admission he had noticed an increased awareness of gastric fullness after taking fluids or small meals.

The chest X-ray on admission showed marked elevation of the left hemidiaphragm, some cardiac enlargement, fibrosis and calcified foci in the left upper lobe of the lung (*Fig.* 1). A barium meal performed 48 hours after admission showed an elevated stomach with a 'cup and spill' deformity but no evidence of peptic ulceration (*Fig.* 2).

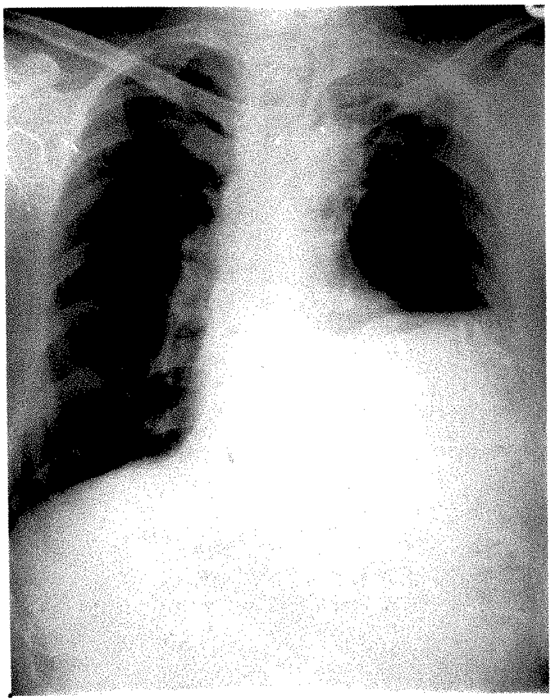


Fig. 1. Chest X-ray showing marked left diaphragmatic elevation.

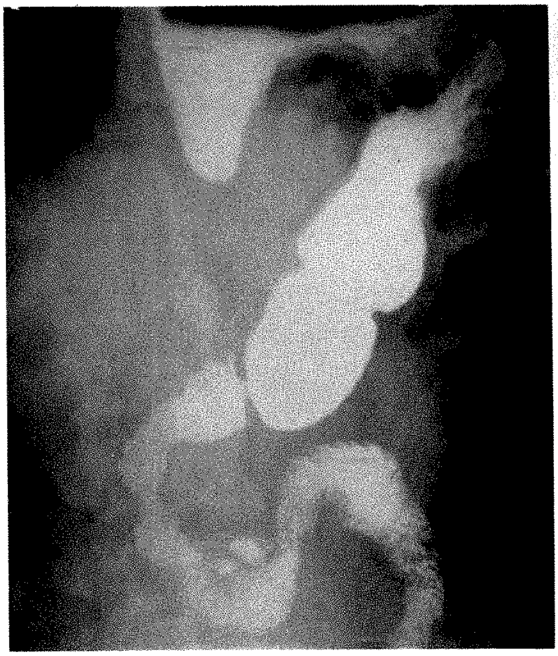


Fig. 2. Barium meal film showing 'cup and spill' gastric deformity.

Six days after admission the patient had a massive haematemesis and melaena and became severely shocked. The haemoglobin dropped to 8 g per cent, and despite an 8-pint transfusion over 3 hours the haemoglobin did not rise. There were difficulties at this stage in acquiring blood owing to the formation of antibodies and it was decided that a laparotomy was indicated.

The abdomen was opened through a right upper paramedian incision. The stomach was enlarged and lying more anteriorly than usual. There was no external evidence of peptic ulceration of the duodenum or anterior gastric wall. The duodenum was inspected through a duodenotomy and appeared healthy, but there was brisk haemorrhage coming from the stomach. The lesser sac was opened and it then became apparent that the gastric fundus had rotated posteriorly and was occupying the lesser sac, pushing the stomach anteriorly (*Figs.* 3, 4). Through a long gastrotomy it was possible to see haemorrhage coming from the opening into the retroverted fundus at the level of the oesophageal opening, but it was not possible to visualize its mucosa because of its fixation to the posterior abdominal wall. Three litres of blood clot and a number of undigested pea skins were retrieved from the fundus. In order to gain access to the fundus the duodenum was divided and the stomach mobilized as far as the oesophagus on the lesser curvature and to above the short gastric vessels on the greater curvature. By elevating the stomach vertically it was possible

---

* Stepping Hill Hospital, Stockport, Cheshire.

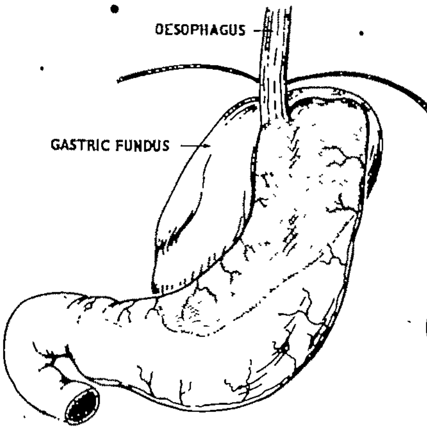


Fig. 3. Anterior aspect of stomach and gastric fundus.

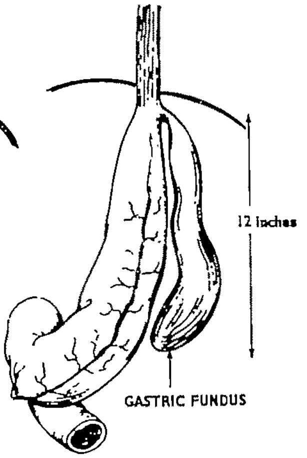


Fig. 4. Left lateral aspect of stomach and empty gastric fundus.

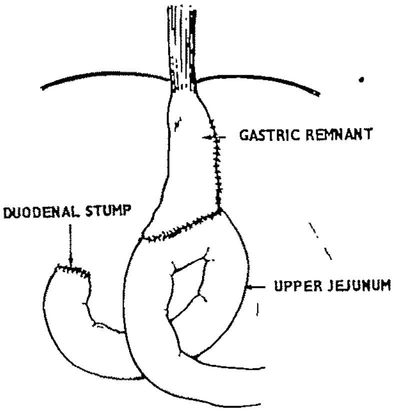


Fig. 5. Completed anatomy after fundectomy and gastrectomy.

to mobilize the fundus from the posterior abdominal wall by blunt dissection. By invagination of the fundus up through the gastrotomy it could be seen that the mucosa was replaced by multiple erosions. The fundus was excised on a level with the oesophageal opening and, as the antral region of the gastric remnant by this stage looked ischaemic, a Polya gastrectomy was also performed. The complete anatomy is depicted in *Fig.* 5.

The postoperative course was delayed by a transient jaundice and a prolonged left basal pneumonia. The patient was symptom-free and back at work at the 5-month follow-up.

Discussion

This case cannot be classified as a true volvulus of the stomach. Usually a volvulus requires the rotation of the greater curvature of stomach around the axis from the gastro-oesophageal opening to the pylorus (organo-axial) or in a plane at right angles to this (mesentero-axial). In the present case only the fundus was involved in a posterior organo-axial rotation.

Anatomical abnormalities associated with gastric volvulus have been summarized by Tanner (1968) and include ligamentous laxity, abnormal bands and adhesions, attraction to abnormal spaces, para-oesophageal hiatus hernia, congenital diaphragmatic hernias and eventration of the diaphragm. Ruckley and Fraser (1968) described a case of volvulus associated with leukaemic splenomegaly. Wastell and Ellis (1971), in their review of the world literature, showed that 80 per cent of cases occurred idiopathically and the remainder were related to anatomical defects. They included a case associated with an omental ball following previous surgery. In this case there was marked diaphragmatic elevation and the dimensions of the fundus were greatly increased. It is possible that the combination of these two factors was responsible for the volvulus.

Gastric volvulus may be asymptomatic or present as an acute surgical emergency with signs of acute obstruction or strangulation (Leading article, 1971). Haemorrhage as a presenting sign is rare, and the common symptoms are severe epigastric pain and Borchardt's triad (1904), namely vomiting followed by retching and finally inability to vomit, epigastric distension and inability to pass a nasogastric tube. Radiologically, barium fails to negotiate the oesophagogastric junction. In the present case none of these criteria was fulfilled and although barium passed into the stomach the true outline and dimensions of the fundus were obscured by the massive amount of blood clot that it contained.

It is postulated that the erosions were caused by stagnation as the pea skins retrieved at operation were eaten 10 days before surgery.

Technically, because the diaphragm and the stomach were elevated a thoraco-abdominal approach would have simplified access and mobilization of the fundus, and a gastrectomy may well have been avoided. In view of the previous tuberculosis, concomitant fibrosis and paralysed diaphragm it was considered that a thoracotomy would have imposed an excessive burden on an already extremely ill patient.

Acknowledgement

I should like to thank Mr G. R. Carr for his permission to publish this case and for his helpful advice and criticism.

References

BORCHARDT M. (1904) Zur Pathologie und Therapie des Magenvolvulus. *Arch. Klin. Chir.* 74, 243–260.

LEADING ARTICLE (1971) Volvulus of the stomach. *Br. Med. J.* 4, 446.

RUCKLEY C. V. and FRASER J. (1968) Gastric volvulus and hiatus hernia. *J. R. Coll. Surg. Edinb.* 13, 217–225.

TANNER N. C. (1968) Chronic and recurrent volvulus of the stomach with late results of "colonic displacement". *Am. J. Surg.* **115**, 505–515.

WASTELL C. and ELLIS H. (1971) Volvulus of the stomach. *Br. J. Surg.* **58**, 557–562.

Br. J. Surg. Vol. 62 (1975) 226–230

Is 'second look surgery' justified in suspected recurrences of cancer of the stomach?

HAROLD ELLIS AND G. JAYASEKARA*

SUMMARY

A series of 23 patients with suspected recurrent disease following 'curative' resection for gastric carcinoma was submitted to further laparotomy (24 operations). Three patients were found to have hopeless dissemination, 10 had palliative procedures performed which relieved their dysphagia, vomiting and jaundice, 4 had recurrences resected and 1 had a second primary of the gastric stump excised. No less than 6 were found to have benign lesions.

Although the reward as far as prolonged survival is small, we believe that the relief of symptoms and the occasional long term excellent result justifies judicious use of a 'second look' laparotomy for suspected recurrent disease.

THE development of clinical features which suggest the recurrence of disease following what was believed to be a curative cancer resection is a depressing state of affairs which until recently was regarded by most surgeons as an entirely hopeless situation. However, in the past few years it has become increasingly recognized that some cancers have a tendency to local recurrence which may be controlled by further radical surgery, or that the apparent recurrence is in fact the development of a second primary metachronous tumour, which itself may be entirely operable. In some instances the clinical features may indeed be produced by altogether benign and curable situations, for example, a granulomatous stricture at an anastomosis. It is particularly in cancers of the colon and rectum that such favourable situations are likely to be found, and this we have recently reviewed (Ellis, 1974). However, most surgeons regard recurrent disease following resection of a gastric or oesophageal cancer as carrying a particularly poor prognosis.

This paper presents the results of a policy, carried out over the past 10 years, of re-exploring the abdomen for suspected recurrent cancer following 'curative' resections of gastric and oesophageal tumours in patients in whom the clinical features do not suggest that widespread hopeless dissemination of the disease had taken place. During this time 23 patients have been subjected to further laparotomy (24 operations). Of these, 20 had had their primary operation carrried out in the Surgical Unit, Westminster Hospital, and the remaining 3 were referred from other hospitals.

In carrying out this second exploration we had the following four possibilities in mind:

1. Could the clinical features be due to some altogether benign and remediable lesion?
2. If not, might a metachronous, resectable cancer have developed?
3. If indeed the tumour had recurred, could this itself be resected?
4. If the recurrence was unresectable, would a palliative short circuit or intubation to relieve obstruction be worth while?

Findings at operation

The findings in our 24 operations are shown in *Table I.*

Table I: FINDINGS AT 'SECOND LOOK' SURGERY

Finding:	No. of cases:
Benign lesion	6*
A second primary in the stomach	1
Recurrence in the gastric stump resected	3
Resection of ovarian secondary	1
Palliative procedure	10†
Laparotomy only	3

* One patient was subsequently re-explored for recurrence.
† One patient had undergone a previous laparotomy for a benign lesion.

Benign lesions mimicking recurrent disease (6 patients)

Two patients developed a benign stricture which radiologically mimicked recurrent cancer; both underwent re-resection. The first patient remains well 2 years following resection of his post-oesophagectomy stricture; the second died of disseminated cancer only 8 months after resection of his benign stricture following a total gastrectomy.

Two patients were re-explored for vomiting and pain which developed after partial gastrectomy. The first was found to have a benign stomal ulcer and was submitted to vagotomy; she remains well 4 years later. The second patient had a Roux conversion which relieved his symptoms but he developed disseminated recurrences and died 1 year following his second operation.

One patient presented with a mass in his abdominal scar, vomiting and loss of weight 5 months after total gastrectomy. The second laparotomy revealed that the mass was a sterile chronic abscess in the abdominal wall and his abdominal symptoms were produced by obstructing postoperative adhesions affecting the upper jejunum. These were divided and he remained well for 4 years. He then developed an anastomotic recurrence with dysphagia. This was treated by a Souttar's tube intubation and he died 1 month following this.

One patient from Cyprus presented with vomiting and dysphagia 4 months after an upper partial gastrectomy for a carcinoma of the cardia performed at another hospital. At laparotomy there was no evidence of recurrent disease. A pyloroplasty was performed and her symptoms disappeared. The patient returned to Cyprus and has been lost from our follow-up.

---

* Surgical Unit, Westminster Hospital, London.

In this group 3 patients achieved reasonably long term satisfactory results, 2 of whom are still living, 2 patients developed recurrences quite rapidly and 1 has been lost to follow-up.

A second primary in the stomach
There was 1 example in this series of an undoubted metachronous primary in the stomach. This was a female patient who in 1943, at the age of 43, had a partial gastrectomy for a spheroidal cell carcinoma of the stomach. She returned in 1967 at the age of 67 with a tumour mass in the gastric stump and an abdominal total gastrectomy was performed. Histological examination revealed a highly anaplastic carcinoma which did not resemble the appearance of the original tumour. The lymph nodes were extensively involved. Local recurrences rapidly developed and she died 6 months after her second operation.

Resection of recurrences (4 patients)
Three patients developed local recurrences which were resectable; 1 after partial gastrectomy and 2 after total gastrectomy. The partial gastrectomy was converted to total gastrectomy but recurrences developed and the patient died 11 months later. One of the patients who had undergone total gastrectomy died only 4 months after resection of the anastomotic recurrence. The other patient remained well for 20 months following this procedure; he then developed a further local recurrence which was treated by radiotherapy and he has remained clinically free from disease for 3 years.

The fourth patient developed an ovarian metastasis 1 year after her partial gastrectomy. This was resected but she died 14 months later with widespread metastases.

Only 1 of the 4 patients in this group has had reasonable long term benefit from surgery although 2 others were relieved of their dysphagia.

Palliative operations (10 patients)
Four patients with dysphagia due to local recurrences following partial or total gastrectomy had the obstruction intubated by means of a Porge's or Souttar's tube. Although dysphagia was relieved, these patients died 3 weeks, 3 weeks, 6 weeks and 2 months respectively following the procedure.

In 3 patients a gastro-enterostomy was performed to the gastric stump; obstructive symptoms were relieved but the patients died 3, 5 and 8 months respectively following surgery.

Three patients developed obstructive jaundice due to tumour masses in the porta hepatitis and it was possible to short-circuit the distended gallbladder to the jejunum. Jaundice was relieved but the patients died 6 weeks, 2 months and 7 months respectively after this second operation.

Laparotomy only (3 patients)
In 3 patients laparotomy was performed with the discovery of widespread intra-abdominal dissemination. One patient died 4 days postoperatively. The others were treated with 5-fluorouracil but died 7 weeks and 7 months respectively following laparotomy.

Discussion

Results of previous re-exploration programmes
An important stimulus to surgical thinking on the problem of recurrent abdominal cancer was the interesting and controversial work of Wangensteen, who introduced his 'second look' programme in 1948 (Wangensteen, 1949). In this experiment, patients who had undergone what was considered to have been curative resection of the stomach or large bowel, and in whom the regional lymph nodes were found to be involved on histological examination, were re-explored approximately 6 months later. At this 'second look' any recurrence of cancer, if found, was resected if this was technically possible. Subsequently, similar operations were performed on the patients in whom further tumour had been found and resected, and these were repeated at intervals of 6 months to 1 year until either no further tumour was discovered or the situation was obviously out of control. Once the patient had had an exploration which revealed no residual cancer, further laparotomy was not performed but careful follow-up was continued. Within a few years it was obvious that although results of re-exploration in colonic cancer were encouraging, rectal cancer recurrences tended to be diffuse and reoperation in gastric cancer was difficult and far less rewarding (Wangensteen et al., 1954).

An extensive survey of the results of this programme up to July 1967 was published by Griffen et al. in 1969. In the group of patients with carcinoma of the stomach 64 were submitted to re-exploration. Twenty-eight of these had a negative 'second look', of whom 10 subsequently developed recurrent cancer, 7 died of other causes and 11 remained alive and well. Of 37 patients with positive 'second look' operations, there were 3 operative deaths, 1 patient died of causes other than cancer and 31 developed further recurrent disease. Only 2 patients were alive and well and could therefore be considered to have been 'converted' to this state by the additional resection. In this study a further 37 patients were reported who presented with symptomatic recurrent disease and were re-explored; none of these was converted to a cancer-free situation. These figures therefore gave no support to a continued programme of elective re-explorations in gastric cancer.

In the past 20 years there have been other important studies of series of recurrent gastric carcinomas subjected to further laparotomy with re-resection, where this was possible. In addition to these reviews there has been a considerable number of individual case reports. These papers, on the whole, paint a gloomy picture of the prognosis following a further resection, but there are occasional brilliant results with survival of 5 or more years following the second operation.

Bowden et al. (1954) described 37 patients who were re-explored for recurrent gastric carcinoma; in 15 a further resection was carried out. There were 2 postoperative deaths. Of the 13 recovering from surgery, 8 patients survived an average of 8 months, 2 were alive with metastases, 2 were alive and clinically clear of disease at 15 and 18 months and 1 patient was alive and well 5 years and 10 months following the second operation. Of the 22 patients in which further resection was impossible, 4 underwent palliative procedures. The average survival in these 22 patients was 6 months with a range of 1–20 months. Welch and Wilkins (1958) carried out 7 'second look' gastric cancer operations; in 4 it was possible to carry out further resection, and although 2 of the patients died postoperatively, the other 2 lived for 5 years after the second operation. It is interesting that neither of these had positive lymph nodes at either laparotomy. Funderburk (1962) collected reports on 53 patients undergoing reoperation for cancer of the stomach, including 2 of his own cases. Resection was possible in 24 of these patients, with survival of 4–70 months; 6 lived for more than 18 months. One of his own patients had a partial gastrectomy in 1946 which was converted in 1957 to total gastrectomy for recurrence. In 1961 she had a third operation in which a malignant node in the jejunal mesentery was resected and she was alive at the time of reporting. Ferguson and Nusbaum (1963) reviewed 94 patients undergoing primary surgery for cancer of the stomach; 93 were explored and 48 underwent radical gastrectomy. Two of these were subsequently re-explored for recurrent disease; one recurrence was resected 7 years later and the patient was well 4 years after the second operation; another patient developed a metastatic lesion in the colon which was resected 8 years after the initial surgery, but the patient died 3 years later of recurrent disease. Lippert (1968) reported 5 cases of reoperation for gastric cancer; 3 underwent radical re-resection; 1 of these died 3 years after the second operation, but the other 2 were alive at 4 and 7 years. The fourth patient underwent a decompression operation for common bile duct obstruction and died 30 months later. The fifth patient underwent a total of 4 'second look' procedures over the course of 2½ years—resection of small bowel, removal of deposits first in the left and then in the right ovary and finally an ileotransverse colon bypass operation. The patient died 2 months after the short-circuit procedure.

Iwasa et al. (1972) have recently reported an extensive study of operations for recurrent gastric cancer in Tokyo, with overall discouraging findings; 109 patients were seen between 1956 and 1971 with recurrent tumours. Of these, 58 were submitted to a second laparotomy. Four only were suitable for further resection and only 1 of these survived for 2 years. Fifteen patients were submitted to laparotomy only, and the rest had various palliative procedures, including bypass or feeding jejunostomy. Most of these were dead within 1 year.

An extraordinary case was reported by Aviles (1973); this woman underwent a right hemicolectomy for carcinoma in 1942, a resection of a second tumour in the sigmoid colon in 1946, a partial gastrectomy for a carcinoma of the stomach in 1960 (at which time the lymph nodes were clear) and in 1967 a total gastrectomy for recurrence in the stump. The patient recovered from this procedure but no further information was given about her subsequent progress.

Tumour implantation

It is well known that tumour cells may seed into the wound at the time of operation (Ryall, 1907). Such deposits may occur not only after surgical exploration but even at the site of paracentesis for malignant ascites (Bush, 1957). Such implantation may be widespread throughout the abdominal wound and peritoneal cavity, but occasionally isolated deposits may develop which are suitable for excisional surgery. Ackerman and Wheat (1955) described a patient who was well 4 years after a resection of a tumour mass in the abdominal scar which developed 1 year following resection of a gastric carcinoma. Sonneland (1959) resected a scar deposit 2 years after gastrectomy for a carcinoma of the stomach. The patient was alive 1 year later but had liver deposits. Fortner and Lawrence (1960) reviewed the extensive experience at the Memorial Hospital for Cancer, New York. 'Curative' gastric resections were carried out on 569 patients between 1931 and 1957. Eleven of these subsequently developed a lump in the laparotomy scar and it is interesting that 2 of these were benign, one being a desmoid, the other an inflammatory mass. Of the 9 secondary deposits, 3 were excised, 2 had radiotherapy and 4 had no local treatment. All these patients died with carcinomatosis 3–28 months after the recurrence.

In 1958, in a survey of 31 patients having laparotomies for suspected recurrent cancers, we reported a patient who had recurrences removed from the abdominal scar 7 and 17 months following resection for gastric carcinoma. Four months after the second recurrence had been removed she developed deposits in both axillae which were excised; she died some months following this from carcinomatosis (Cronin and Ellis, 1958).

A striking long term survival was reported by Inouye and Erb (1965); this was a patient who underwent a partial gastrectomy in 1945, developed a deposit in his abdominal incision 3 months later and then survived after its excision for 17 years until 1963, when he developed a recurrence in his gastric stump and died following further resection.

Metachronous cancer in the gastric stump

A second carcinoma developing in the same organ is a well-recognized phenomenon, particularly in squamous and basal tumours of the skin, in carcinomas of the large bowel and, in a slightly different context, in the opposite breast following mastectomy. A second primary cancer may also undoubtedly develop in the gastric stump following partial gastrectomy for malignant disease. In this situation the development of a second primary tumour must be differentiated from recurrence of the original disease, and can be made on the grounds either that the two tumours are quite distinct in histological appearance or that the interval between the appearance of the two tumours is sufficiently long to make recurrence of the original cancer unlikely. Morgenstern (1960), in presenting 2 such patients, was able to review 11 previously reported cases. Five of these had no follow-up, 5 died at intervals of up to 14 months following operation and 1 patient lived for 7 years after the second resection (Stoloff and Lattimore, 1955).

In a later paper Morgenstern et al. (1973) were able to add 2 more patients to Morgenstern's original experience. They considered that a gap of no less than 20 years should elapse between the two tumours in differentiation between recurrence and a second primary cancer, although other authors accept a gap of 10 years. Of the 4 patients reported, 1 initially had a partial gastrectomy for a reticulum cell sarcoma and died 4 years after resection of an adenocarcinoma arising in the stump 25 years after the initial operation. The other 3 patients, all of whom had an initial carcinoma of the stomach and who subsequently developed a second tumour 22, 25 and 30 years later respectively, underwent further resection. There was 1 postoperative death, 1 patient died 2 years after the second operation and 1 patient was still alive and well 5 years later.

Obviously, the development of a second cancer of the stomach following partial gastrectomy is an unusual occurrence, probably related, at least in part, to the fact that prolonged survival following gastrectomy is unfortunately an infrequent phenomenon. In the patient we reported the interval between the two operations was 24 years and the histological appearance of the two tumours was entirely dissimilar so that undoubtedly this represented a metachronous primary cancer. Unfortunately rapid recurrence and death followed the second resection.

Conclusion

Carcinoma of the stomach remains one of the most dangerous of the major cancers and is the third commonest cause of death from malignant disease in the United Kingdom. In patients undergoing what is thought to be curative resection, large numbers present with obvious clinical recurrent disease within 5 years.

There is a general feeling among surgeons that when recurrence or metastases are diagnosed following gastric resection the situation is a hopeless surgical proposition. A review of previous publications and of our own experience confirms that the outlook is indeed gloomy, but by no means hopeless. In the 23 patients we have operated upon over the past 10 years (24 operations) 3 had a laparotomy only, confirming a hopeless situation. Ten had palliative procedures for obstructive jaundice, gastric outlet obstruction or dysphagia, and all of these died within a few months, although useful palliation had been achieved from these unpleasant symptoms. Four patients with recurrent or metastatic disease were suitable for resection, but only 1 achieved 3 years of relief of his dysphagia, and this period included a course of radiotherapy for further recurrent disease. One patient with an undoubted metachronous lesion in the gastric stump died 6 months after further resection. However, it must be noted that from time to time encouraging long term survivals have been reported following re-resection of recurrent, metastatic and metachronous cancers after gastric resection.

Perhaps the brightest ray of encouragement is our finding that no less than 6 of our patients who were considered clinically to have developed recurrent disease were found to have benign lesions at laparotomy. One has been lost to follow-up, 2 are well 2 and 4 years after surgery respectively, but the remaining 3 developed frank recurrent disease and died 8 months, 1 year and 4 years respectively following the finding of a benign lesion at their 'second look' procedure (the last patient having intubation performed for his recurrent tumour).

In spite of this small reward we conclude that a laparotomy is still justifiable in a patient who develops clinical evidence of apparent recurrent disease following 'curative' resection for gastric cancer. Rarely an altogether benign lesion can be found and cured, and perhaps this alone is worth all the endeavour. Occasionally a recurrent or metachronous lesion can be resected with long term cure, although this was not our own experience in this small series. There is no doubt that in many cases unpleasant symptoms (dysphagia, gastric outlet obstruction and jaundice) can be relieved up to the time of the patient's death, even though this may be measured only in months or even weeks.

However, even if nothing at all can be done at the time of surgery, at least the diagnosis can be confirmed without any doubt, a decision made as to whether or not cytotoxic drugs should be employed and, perhaps most important of all, the patient's family and the patient himself can realize that no stone has been left unturned before the final hopeless prognosis has been given.

References

ACKERMAN L. V. and WHEAT M. W. (1955) The implantation of cancer—an avoidable surgical risk? *Surgery* **37**, 341–355.

AVILES E. (1973) Late recurrent gastric carcinoma. *Int. Surg.* **58**, 56–57.

BOWDEN L., BOOHER R. J. and MCNEER G. (1954) Recurrent gastric carcinoma: an interim evaluation of surgical results. *Surgery* **38**, 204–211.

BUSH A. K. (1957) The surgical implantation of tumours. *Am. Surg.* **23**, 1012–1021.

CRONIN K. AND ELLIS H. (1958) The problem of suspected recurrences in cancer of the alimentary tract. *Br. Med. J.* **2**, 1319–1321.

ELLIS H. (1974) Second look surgery for suspected recurrences in cancer of the large bowel. *Cancer Treatment Rev.* **1**, 205–220.

FERGUSON L. K. and NUSBAUM M. (1963) Survival after surgical treatment of cancer of the stomach. *Ann. Surg.* **158**, 51–55.

FORTNER J. G. and LAWRENCE W. (1960) Implantation of gastric cancer in abdominal wounds. *Ann. Surg.* **152**, 789–794.

FUNDERBURK K. W. W. (1962) Survival following re-operation for cancer of the stomach. *J. Natl Med. Assoc.* **54**, 80–85.

GRIFFEN W. O., HUMPHREY L. and SOSIN H. (1969) The prognosis and management of recurrent abdominal malignancies. In: *Current Problems in Surgery* (April). Chicago, Year Book, p. 3.

INOUYE W. Y. and ERB W. H. (1965) Seventeen year survival after removal of recurrent gastric carcinoma. *Am. J. Surg.* **109**, 656–658.

IWASA H., IMAMURA K., ISHII T. and SEKIZUKA H. (1972) Studies on operations of recurrent gastric cancer cases. *Bull. Tokyo Med. Dent. Univ.* **19**, 237–244.

LIPPERT G. G. (1968) Re-operation for gastric carcinoma. *Can. Med. Assoc. J.* **98**, 604–607.

MORGENSTERN L. (1960) The late development of gastric cancer after gastrectomy for malignant disease. *Surgery* **47**, 557–567.

MORGENSTERN L., YAMAKAWA T. and SELTZER D. (1973) Carcinoma of the gastric stump. *Am. J. Surg.* **125**, 29–37.

RYALL C. (1907) Cancer infection and cancer recurrence: a danger to avoid in cancer operations. *Lancet* **2**, 1311–1316.

SONNELAND J. (1959) Accidental seeding of cancer in the operative scar. *Northwest Med.* **58**, 1687–1692.

STOLOFF I. L. and LATTIMORE T. J. (1955) Episodic stomach cancer. *Ann. Intern. Med.* **42**, 1284–1288.

WANGENSTEEN O. H. (1949) Cancer of the colon and rectum. *Wis. Med. J.* **48**, 591–597.

WANGENSTEEN O. H., LEWIS F. J., ARHELGER S. W., MULLER J. J. and MACLEAN L. D. (1954) An interim report upon the 'second-look' procedure for cancer of the stomach, colon and rectum and for 'limited intraperitoneal carcinosis'. *Surg. Gynecol. Obstet.* **99**, 257–267.

WELCH C. E. and WILKINS E. W. (1958) Carcinoma of the stomach. *Ann. Surg.* **148**, 666–681.

Br. J. Surg. Vol. 62 (1975) 231–233

Flatulent dyspepsia in patients with gallstones undergoing cholecystectomy

R. D. KINGSTON AND C. W. O. WINDSOR*

SUMMARY

The incidence of flatulent dyspepsia and its relationship to gallbladder function has been studied in 100 consecutive patients with gallstones undergoing cholecystectomy. Thirty-three per cent of patients suffered significant flatulent dyspepsia of whom 80 per cent were cured or improved by operation.

In 15 patients gastric function was studied pre- and postoperatively and it was noted that there was no difference in gastric emptying times between patients with flatulent dyspepsia who were cured by operation and those who remained symptomatic.

Bacteriological studies on gallbladder bile from 39 patients suggested that infection within the gallbladder may be a factor in the causation of flatulent dyspepsia.

IT is not uncommon to have to decide whether the removal of a non-functioning gallbladder will cure the symptoms of flatulent dyspepsia or conversely whether cholecystectomy will cure flatulent dyspepsia in a patient with a normal cholecystogram. These difficulties arise because the symptom complex known as flatulent dyspepsia is often ill-defined and because the cause of the symptoms is not fully known. Certain of the clinical features—fullness after meals, distension and nausea—are suggestive of gastric retention, whilst others—retrosternal discomfort and bilious vomiting—suggest oesophagitis and a hiatus hernia.

In this study gastric emptying has been measured before and after cholecystectomy and the findings related to the symptoms of flatulent dyspepsia. Also, correlations between other factors such as gallbladder function and biliary infection have been sought.

Materials and methods

This is a prospective study of 100 consecutive patients undergoing cholecystectomy for gallstones. There were 75 females and 25 males. The average age was 53 years with an age range of 17–80 years. The follow-up was between 3 months and 3 years with a mean of 13 months. All the patients were interviewed pre- and postoperatively.

A patient was considered to have flatulent dyspepsia if three or more of the following symptoms were consistently present to a moderate or severe degree. A combination of the last three symptoms *only* was not classified as flatulent dyspepsia.

Symptoms

Flatulence: Repeated belching; full feeling after a normal-sized meal; inability to finish a normal-sized meal; abdomen becomes blown out so that clothes need to be loosened.

Dyspepsia after meals: Burning discomfort in the epigastrium; burning discomfort in the chest; vomiting or nausea.

All symptoms were noted preoperatively and at review 3–12 months postoperatively.

Gallbladder function was assessed by oral cholecystography in 83 patients; Biliodyl (phenobutiodil) 0·3 g/kg body weight was given 12 hours before X-ray.

Bile from the gallbladder in the last 39 patients in the series was sent directly from the operating theatre for culture.

Pre- and postoperative gastric emptying times were measured in 15 patients: 5 flatulent dyspeptics who were cured by operation, 5 who were not cured and 5 patients not suffering with flatulent dyspepsia. The patients ate a meal consisting of two slices of bread and butter (1 oz), two scrambled eggs, a cup of tea and 30 ml of Raybar (barium). The ingredients were liquidized. After ingestion X-rays were taken at 15-minute intervals for 2 hours and 30 minutes thereafter. Three times were recorded: (*a*) the start of gastric emptying; (*b*) the time when the head of the meal reached the caecum; (*c*) the time when gastric emptying was completed.

The patients were encouraged to sit in a chair or to stroll about in the intervals between X-rays. The postoperative measurements were made between 6 and 12 weeks after operation.

Table I: REFERRING SYMPTOM

Symptom:		No. of cases:
	Acute cholecystitis	52*
	Biliary colic	28
	Jaundice	11
	Flatulent dyspepsia	4
	Incidental	3
	Pancreatitis	2
	Total	100

* Four perforated gallbladders.

Results

A review of the symptoms leading to the patients' referral is shown in *Table I*, only 4 per cent of patients presenting primarily with flatulent dyspepsia. However, 33 of the 100 patients reviewed had significant flatulent dyspepsia, and 27 (80 per cent) of these were cured or improved of their symptoms by cholecystectomy.

Analysis of gallbladder function in the two main groups of patients—flatulent dyspeptics and non-dyspeptics—reveals that there were more functioning than non-functioning gallbladders in the patients with

---

* Worcester Royal Infirmary.

Table II: GALLBLADDER FUNCTION IN 83 PATIENTS BEFORE OPERATION

Group	Non-functioning gallbladder No.	Non-functioning gallbladder %	Functioning gallbladder No.	Functioning gallbladder %
Concentration				
Dyspeptics*	13	43	17	57
Non-dyspeptics	27	52	26	48
Contraction				
Dyspeptics†	14	47	16	53
Non-dyspeptics	31	59	22	41

*$\chi^2 = 1{\cdot}91$.
†$\chi^2 = 0{\cdot}6$.

Table III: GALLBLADDER FUNCTION IN 30 PATIENTS AFTER OPERATION

Group	Non-functioning gallbladder	Functioning gallbladder
Concentration		
Cured dyspeptics*	11	15
Non-cured dyspeptics	3	1
Contraction		
Cured dyspeptics†	9	17
Non-cured dyspeptics	3	1

* $\chi^2 < 0{\cdot}46$.
† $\chi^2 < 0{\cdot}97$.

Table IV: BACTERIOLOGICAL FINDINGS OF BILE CULTURED FROM THE GALLBLADDER IN 39 PATIENTS

Group	Infected bile	Non-infected bile
Dyspeptics	8	5
Non-dyspeptics	13	13
Cured dyspeptics	7/8	—
Non-cured dyspeptics	0/5	—

flatulent dyspepsia (*Table II*). Further, in comparing gallbladder function (*Table III*) in dyspeptics cured by operation and those remaining symptomatic postoperatively there were more functioning than non-functioning gallbladders in patients who were cured of their dyspepsia. In neither group, however, is the difference statistically significant ($\chi^2 = 1{\cdot}91$, 0·6, 0·46, 0·97).

Table IV correlates the symptoms of flatulent dyspepsia with the bacteriological findings of the bile taken at operation from the gallbladder. In the non-dyspeptic group equal numbers of patients (13) had infected and non-infected bile. In the dyspeptic patients 8 patients had infected bile and 5 had sterile bile. Seven out of 8 patients cured of their dyspepsia by operation had infected bile, whilst the bile was sterile in those whose symptoms remained (5 patients).

Fig. 1 shows the results of the gastric emptying studies in the three groups of patients studied pre- and postoperatively—those cured of flatulent dyspepsia, those not cured of flatulent dyspepsia and a group of patients not having symptoms of flatulent dyspepsia. Five patients were studied in each group and the results are the means of the times. Gastric emptying (column 1) commenced in the first 15 minutes in all groups and was not influenced by operation. Column 2 shows the times taken for the meal to reach the ileocaecal valve. Cholecystectomy seemed to increase this transit time, particularly in patients whose dyspepsia was not improved by operation. Column 3 shows the time taken for complete gastric emptying, which is similar in all three groups and not altered postoperatively except slightly lengthened in the non-cured dyspeptics. In summary, there was no significant difference in emptying times in the three groups studied and operation made very little difference to the emptying times.

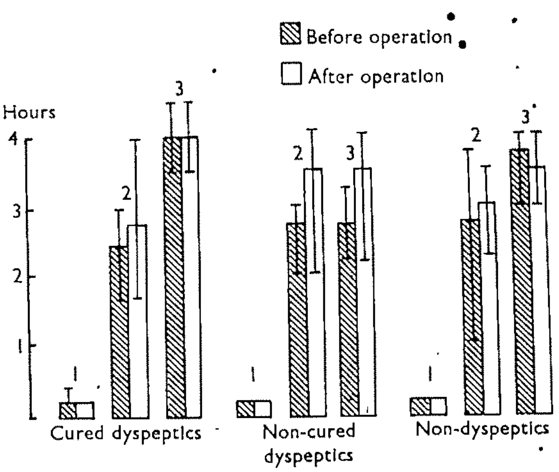


Fig. 1. Gastric emptying times before and after operation in patients who were cured of flatulent dyspepsia by operation, those not cured by operation and patients without symptoms of flatulent dyspepsia.

Discussion

In 1971 Johnson performed a pre- and postoperative symptomatic review of 108 patients undergoing cholecystectomy and related his findings to gallbladder function. He found that preoperatively 83 per cent of his patients suffered with flatulent dyspepsia, which is at variance with our figure of 33 per cent. The explanation is probably that we have been more selective in our choice of patients with flatulent dyspepsia, by excluding those with mild dyspepsia and those with dyspepsia only related to acute cholecystitis. Our objective was to select only patients with a definitely abnormal degree of flatulent dyspepsia.

Our cure or improved rate is similar to that in Johnson's series but not in agreement with Maingot's (1956) statement that cholecystectomy has little or no effect in curing the unpleasant symptoms of flatulent dyspepsia.

Johnson (1971) made two further points: that functioning gallbladders were more common in patients cured of their dyspepsia, and that since removal of the gallbladder cures or improves the majority of patients then the underlying cause must be gallbladder disease. Our findings are in general agreement with these points, but the number of functioning gallbladders in our cured dyspeptics is not statistically significantly higher than that of non-functioning gallbladders.

Capper in 1967 studied pyloric function in patients undergoing cholecystectomy before and after operation by intubation tests and showed that a duodenum distended with bile predisposed to delayed gastric emptying and bile regurgitation (Capper, 1967; Capper et al., 1967). Further, at gastroscopy on these patients he noted a high incidence of gastric atrophy. Johnson (1972) studied pyloric function in three groups of patients—patients with cholelithiasis with and without flatulent dyspepsia and patients with normal cholecystograms and no dyspepsia. He used a modified pyloric regurgitation test, assessing function radiologically and biochemically. A close correlationship between the symptoms of flatulent dyspepsia and pyloric regurgitation was noted in all three groups.

It was these findings which encouraged us to measure gastric emptying times in the three groups of patients and to assess any postoperative difference. The method we used is a simple physiological one which will demonstrate quite small differences in emptying rates. Humphrey and Williamson (1972) using the same technique showed significant differences in gastric emptying times in patients after highly selective, selective or truncal vagotomy. The fact that we did not elicit any difference in emptying times may possibly be accounted for by lack of sufficient stimulus in the meal and the fact that we examined patients in 'remission'. With regard to the periodicity of symptoms it became apparent to us during our study of patients' symptomatology that flatulent dyspepsia in patients with gallstones has exacerbations and remissions. At times dyspeptic patients may comfortably tolerate high fat content meals. In a separate study we fed individual patients up to ten graded fatty meals preoperatively and assessed their dyspepsia. Some patients consistently tolerated high fat meals and yet had suffered severe exacerbations of flatulent dyspepsia previously. It is regretted that only 15 out of the 100 patients underwent gastric emptying studies but in a busy general hospital facilities were not available to study more patients. However, further studies of emptying times are being performed, varying the type of meal, the symptomatic condition of the patient and possibly the method of measurement.

The finding that 7 out of 8 patients with flatulent dyspepsia and infected bile were cured by cholecystectomy is suggestive that infected bile is a factor in the causation of flatulent dyspepsia. Against this is the fact that half of the non-dyspeptic patients had infected bile. It may be a matter of degree and a certain type or level of infection needing to be present before becoming significant in producing flatulent dyspepsia. There did not appear to be a predominant organism responsible for infection in the bile. In 50 per cent of cases a mixed growth was present. *Escherichia coli* was present in 50 per cent of the total either alone or mixed. Streptococci (non-haemolytic and faecal) were present in 40 per cent of the total. There was a wide variety of other organisms isolated, mainly in individual cases.

Infected bile as a significant factor obviously requires further study, but the concept of a functioning gallbladder emptying infected bile into the duodenum producing an ileus with reflux of bile into the stomach would appear to be a very possible cause of flatulent dyspepsia. The fact that infection may be present in a gallbladder without producing signs of acute cholecystitis is supported by the frequent post-mortem and operative finding of chronically infected fibrosed gallbladders which were unsuspected in life.

In assessing the results of cholecystectomy we noted that 9 out of 10 patients with flatulent dyspepsia and a non-functioning gallbladder were cured or improved by cholecystectomy. Similarly 14 out of 17 patients with flatulent dyspepsia and a functioning gallbladder containing stones were cured or improved by cholecystectomy.

However, during the period of this survey as a result of deliberate policy 6 patients with functioning gallbladders but no stones (therefore not included in this series) having severe flatulent dyspepsia underwent cholecystectomy. In only 2 were the symptoms improved.

References

CAPPER W. N. (1967) Factors in the pathogenesis of gastric ulcer. *Ann. R. Coll. Surg. Engl.* **40**, 21–35.

CAPPER W. M., BUTLER J. J., KILLEY J. O. and GILSON M. J. (1967) Gallstones, gastric secretion and flatulent dyspepsia. *Lancet* **1**, 413–415.

HUMPHREY C. S. and WILKINSON A. R. (1972) The value of preserving the pylorus in the surgery of duodenal ulcer. *Br. J. Surg.* **50**, 779–783.

JOHNSON A. G. (1971) Gallstones and flatulent dyspepsia. Cause or coincidence? *Postgrad. Med. J.* **47**, 767–772.

JOHNSON A. G. (1972) Pyloric function and gallstone dyspepsia. *Br. J. Surg.* **59**, 449–454.

MAINGOT R. (1956) In: ROB C. and SMITH R. (ed.) *Operative Surgery*. London, Butterworth, p. 390.

Br. J. Surg. Vol. 62 (1975) 234–235

Traumatic haemobilia

E. VALLIDIS AND N. PAPALEXANDRIS*

SUMMARY

A case of traumatic haemobilia which was diagnosed preoperatively, is reported. The site of bleeding was demonstrated by operative angiography through the right hepatic artery. The patient was treated by ligation of the common hepatic artery. Re-bleeding required a second operation and ligation of the right hepatic branch without adverse consequences on the hepatic function.

Case report

A 37-year-old man fell off a crane from a height of about 30 ft on the island of Crete. He sustained fractures of the 8th, 9th, 10th and 11th right ribs, rupture of the right lobe of the liver, rupture of the right diaphragm and contusion of the base of the right lung. He was operated on at the local hospital and the ruptured liver and right diaphragm were sutured. His postoperative course was stormy. On the eighth postoperative day he developed jaundice and on the fourteenth day he had melaena which was repeated 2 days later. Twenty-five days after the accident (July 1973) the patient was transferred to the Red Cross Hospital in Athens for further investigation and treatment.

On examination he was found to be in a relatively good general condition with a pulse of 84/minute and a blood pressure of 120/80. He was of light build and slightly pale and his wounds were healed. There was a drain under the right costal margin packed with gauze.

Laboratory investigations showed the following: haemoglobin 86 per cent, ESR 57–83 mm/h, serum bilirubin 2·20 mg per cent, WBC 9600/mm^3, blood urea 0·35 g per cent and urine analysis normal. The chest X-ray demonstrated no other abnormality than fractures of the right 8th–11th ribs with slight displacement of the fractured ends.

On removal of the drain about 1 litre of fluid came out consisting of dark blood, pus, bile and tiny pieces of liver tissue. Culture of the fluid disclosed coliforms sensitive to gentamycin. The body temperature fluctuated from 39·2 to 37·2 °C during the first fortnight after admission.

While the patient's condition was steadily improving and the discharge was diminishing, he suddenly complained of a very severe pain in the right hypochondrium. His pain was relieved by strong analgesics and spasmolytics. A few days later he became jaundiced and had melaenas. Daily haemoglobin estimation showed a sharp drop to 48 per cent despite the transfusion of 1200 ml of blood. An emergency barium meal examination ruled out a gastric or duodenal ulcer as a possible source of bleeding. A sinogram revealed a large liver abscess cavity. Melaenas continued and 1250 ml of blood were required to raise his haemoglobin level to 59 per cent. At that time the diagnosis of traumatic haemobilia was established and the decision to operate was made.

At operation on 13 October 1973 the abdomen was opened through an upper midline incision and the common hepatic artery was ligated at its origin. The patient's recovery was smooth and uneventful. The discharge of blood ceased and his haemoglobin increased to 78 per cent. Postoperative investigations of the liver function proved normal apart from a transitory increase of SGOT and SGPT.

Twenty-four days after the ligation of the common hepatic artery and as the patient was about to be discharged, he complained of excruciating pain in the epigastrium. On examination he was in a collapsed state with a rapid and weak pulse and unrecordable blood pressure. It was obvious that he had severe re-bleeding. After resuscitation he underwent reoperation (6 November).

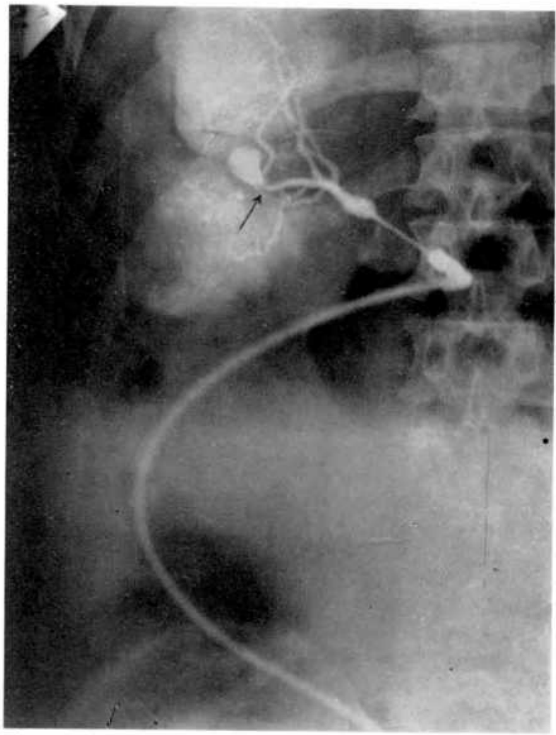


Fig. 1. Right hepatic artery arteriogram. Arrow indicates site of extravasation of opaque medium. This film also demonstrates the fractured ribs and the tube draining the intrahepatic cavity.

The abdomen was opened through the previous incision. The small bowel was full of blood. In order to locate the exact point of bleeding a selective arteriogram was performed by needle puncture through the right hepatic artery (*Fig.* 1). The film taken depicted clearly that the site of bleeding derived from the intrahepatic branch of the right hepatic artery. The right hepatic artery was ligated proximal to the hilus of the liver. His gallbladder and common bile duct were distended by blood clots. Through a cholecystostomy incision the clots of blood were evacuated and a De Pezzer tube was left in position.

The postoperative course was smooth and bleeding stopped. Biochemistry of the liver function was as follows: SGOT 150 u./ml, SGPT 300 u./ml, prothrombin 59 per cent, zinc sulphate test 7·8, alkaline phosphatase 10 KA units.

The patient was discharged on 24 November with his wound completely healed. Three months later re-evaluation of the blood tests gave the following results: haemoglobin 93 per cent, haemocrit 47 per cent, SGOT 65 u./ml SGPT 78 u./ml, alkaline phosphatase 8·9 KA units. The patient's weight had increased by 14 kg to 60 kg.

---

* Second Surgical Department, Hellenic Red Cross Hospital, Athens, Greece.

Table I: SURGICAL PROCEDURES IN TRAUMATIC HAEMOBILIA

1. Lobectomy
2. Ligation of vessels in hepatic cavity
3. Ligation of the common hepatic artery
4. Ligation of branch of the hepatic artery

Discussion

Traumatic haemobilia is a very rare complication of liver trauma. Up to 1968, 31 cases had been reported in the world literature (Wilkinson et al., 1968). Since then we have been able to trace 10 more cases.

The main clinical features of the syndrome are hepatic colicky pain, jaundice and gastro-intestinal bleeding (haematemesis, melaena or both). Undisputable diagnosis can be established by selective arteriography either preoperatively by retrograde catheterization of the hepatic artery or during operation by needle puncture of the same artery. To prevent traumatic haemobilia Turner and Rogers recommended deep sutures for approximation of the traumatized edges of the liver parenchyma. Haemobilia has been reported to occur 2 days to 37 years after hepatic trauma (Caroli, 1959).

Treatment of haemobilia is mainly surgical although conservative treatment has been reported. In *Table I* the various types of operative procedures are listed. Lobectomy has been reported to have a low bleeding recurrence rate although the mortality is increased. Ligation of the bleeding vessels in the hepatic cavity is not always successful and many recurrences have been reported (Wilkinson et al., 1968). Ligation of the common hepatic artery was recommended by Wilkinson et al. (1968). It is a simple procedure, slightly impairing the liver function. Recurrence of bleeding was reported in 3 out of 10 cases. Ligation of the appropriate branch of the hepatic artery should be adequate treatment when the bleeding point has been located by arteriography. Impairment of liver function 3 weeks after ligation of the common hepatic and right hepatic branches was transient in our case.

The high mortality rate with conservative treatment or in undiagnosed cases or in those undergoing irrelevant operative procedures (Manos, 1958; Sandblom, 1972) has been lowered in the past few years as a result of better understanding of the bleeding mechanism and appropriate surgical treatment.

Conclusions

Haemobilia can be diagnosed by the triad of clinical symptoms—colic, jaundice and intestinal bleeding. Preoperative or operative arteriography of the hepatic artery confirms the clinical diagnosis. The treatment is mainly surgical. Of several operative procedures, ligation of the common hepatic artery or ligation of the involved branch has been reported to have a low mortality rate. Bleeding recurs occasionally after common hepatic artery ligation. In our case successive ligation of the common hepatic artery and its right branch has been proved compatible with liver function and survival of the patient.

References

CAROLI J. M. (1959) Hémorrhagies digestives au cours des affections biliaires. *Arch. Mal. App. Dig.* **48**, 1584–1585.

MANOS A. (1958) Rare case of persistent haematemesis and melena (traumatic haemobilia). *Acta Chir. Hell.* **5**, 61–66.

SANDBLOM P. (1972) *Haemobilia.* Springfield, Ill., Thomas.

TURNER G. G. and ROGERS C. L. (1956) *Modern Operative Surgery*, 4th ed. London, Cassell.

WILKINSON G. M., MIKKELSEN W. P. and BERNE C. J. (1968) The treatment of post-traumatic haemobilia by ligation of the common hepatic artery. *Surg. Clin. North Am.* **48**, 1337–1346.

Br. J. Surg. Vol. 62 (1975) 236

Gumma of the liver

ROGER PARNIS*

SUMMARY

A misdiagnosed case of gummatous disease of the liver is described.

Case report

An ex-Army clerk, aged 64 years, who had served in North Africa for some time was admitted to St Luke's Hospital, Malta, on 28 March 1974 on account of epigastric pain of 3 days' duration. There were no other recent symptoms and the pain was not related to food intake, but over the previous 6 months there had been a steady loss of appetite and of weight.

In 1959 the patient had had indigestion for a few weeks and 3 years later an antral ulcer had perforated. The perforation was closed and the patient was put on an ulcer regimen. Since then he had not complained of indigestion. He had lived apart from his wife, who had borne him 10 healthy children, for the past 8 years. The cause of the separation, according to him, was loose living on her part. He smoked 20 cigarettes a day but did not touch alcohol.

When examined the patient was seen to be very thin but was otherwise in good shape. His temperature, pulse rate, respiratory rate and blood pressure were normal. He was not anaemic or jaundiced and his fingers were not clubbed. The pupillary reflexes were normal and his tongue was clean. Abdominal examination showed a tender firm liver containing two nodules and extending three fingers' breadth below the costal margin. No other abnormality was detected and CNS examination was negative.

A provisional diagnosis of carcinoma of the stomach with liver metastases was made. Barium meal examination showed narrowing of the antropyloric region of the stomach. A significant amount of barium was retained after 24 hours. The appearances were suggestive of pyloric obstruction which was probably neoplastic in nature.

At operation two swellings were present in the liver, one in each lobe, measuring about 3 cm in diameter. They were firm but not stony hard and were in the substance rather than on the surface of the liver. The liver was not cirrhotic. The site of the old perforation in the antrum was seen, with adherent omentum, but a thorough examination of the stomach revealed no other abnormality. Liver biopsy was carried out and the abdomen closed. The postoperative course was satisfactory apart from a wound infection which caused a small skin breakdown.

Histological examination revealed gummatous fibrosis; there was a fibroblastic reaction with plasma cell and lymphoid cell infiltration and necrosis. Parenchymal tissue was replaced by the fibrosis. No tumour cells were present.

Further questioning and examination of the patient yielded no history or evidence of a chancre or of other manifestations of syphilis. Serological tests were performed:

1. VD reference laboratory test: strongly positive up to 1 : 16.
2. Reiter protein complement fixation test: strongly positive up to 1 : 640.
3. Kahn test: positive up to 0·0125.

A 3-week course of crystalline penicillin, 1 million units 6-hourly, was given with very good results: the liver swelling markedly decreased, the appetite improved and the patient's weight went up. No Jarisch–Herxheimer reaction was noted. He was discharged 4 weeks after admission and was last seen in September 1974 when the liver was not palpable.

Gumma of the liver is today a very rare condition. The predominant symptoms of loss of weight and of appetite plus the presence of an epigastric tumour make a diagnosis of carcinoma of the stomach almost inevitable.

Acknowledgement

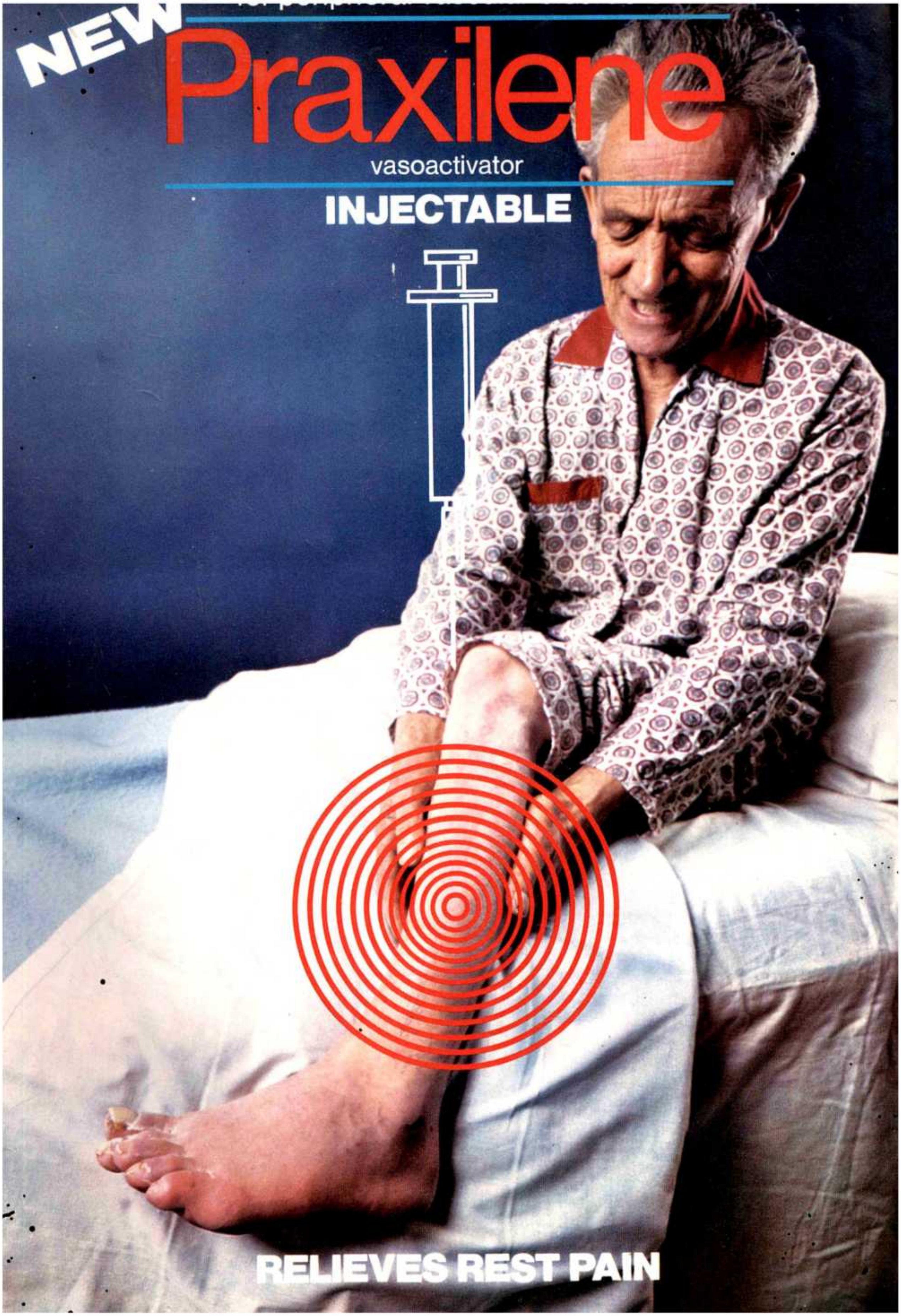
I should like to thank Professor G. P. Xuereb for the biopsy examination.

Reference

KING A. and NICOL C. (1964) *Venereal Diseases.* London, Cassell.

---

* Dar-il-Hena, San Gorg, Birzebbuga, Malta.


NEW
Praxilene
vasoactivator
INJECTABLE
RELIEVES REST PAIN

NEW

for peripheral vascular disorders

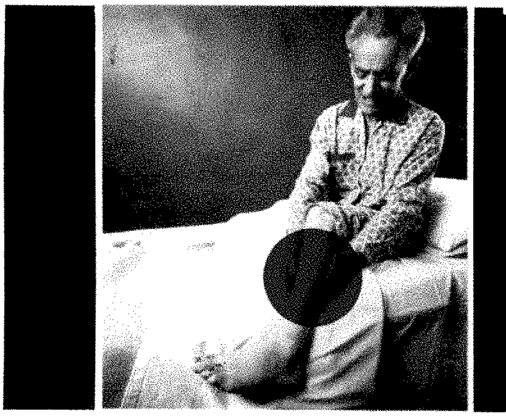
Praxilene

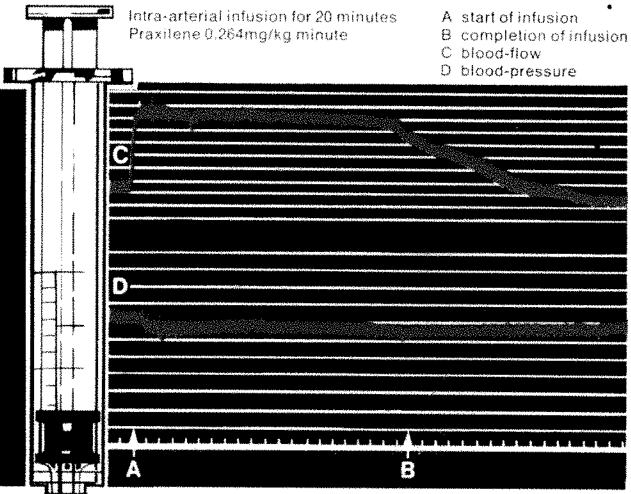
vasoactivator

INJECTABLE

RELIEVES REST PAIN

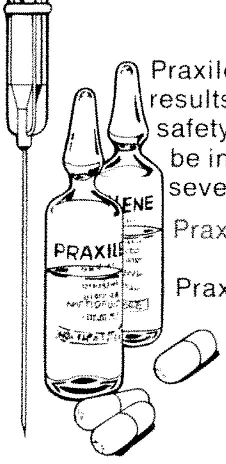
by flushing out pain producing metabolites
by improving blood-flow – without affecting blood-pressure
by a unique metabolic activity





Fast relief
Praxilene administered parenterally (Intra-arterial; Intravenous; Intramuscular) can give relief of pain within as short a time as one week, in many cases.

Prolonged relief
Relief of pain is prolonged: at the same time the collateral circulation is given the opportunity to develop, resulting in an improved blood supply to the affected limb.



Praxilene has produced excellent results because it has a very wide safety margin and the dosage can be individually tailored to the severity of the disorder.

Praxilene: Unique Vasoactivator

Praxilene: Naftidrofuryl: available as 40mg ampoules and 100mg capsules.

Full prescribing information and dosage schedule on request

Lipha (UK)
West Drayton, Middlesex
Telephone: West Drayton 49331/2

Br. J. Surg. Vol. 62 (1975) 237–238

Rupture of subcapsular haematoma of the liver in a case of eclampsia

C. H. BROWNE, GILLIAN C. HANSON, L. R. DE JODE AND P. A. ROBERTS*

SUMMARY

A case of rupture of subcapsular haematoma of the liver in a patient suffering from eclampsia is reported in which the patient survived. Peritoneal tap provided important diagnostic information. Surgical intervention with control of the liver haemorrhage provides the only chance of survival.

RUPTURE of a subcapsular haematoma of the liver is a rare complication of pregnancy. There have been 83 previous case reports in the world literature; a further case is reported here.

Case report

Mrs M. H., aged 22 years, had had a normal full term first pregnancy 2 years previously. She had gained little weight during her present pregnancy, which was otherwise proceeding normally. The blood pressure remained normal. At the 32nd week she was admitted as an emergency to Plaistow Maternity Hospital, with slight vaginal blood loss and lower abdominal pain. On examination her pulse rate was 88/minute, and her blood pressure 150/105 mm Hg. The height of the uterine fundus was compatible with the date and the fetal heart was heard. She was sedated with phenobarbitone and started on oral methyldopa. The same afternoon she went into labour; the fetal heart was no longer heard and she produced a stillborn child. The blood pressure at delivery was 180/110 mm Hg. One hour postpartum her blood pressure had risen to 220/110 mm Hg and she complained of epigastric pain. Pethidine and promethazine were given intramuscularly. Four hours postpartum her blood pressure was 170/120 mm Hg, and she had a convulsion lasting 2 minutes. A chlormethiazole infusion was commenced and oxygen given by mask. She had a further convulsion 65 minutes later when the blood pressure was 110/90 mm Hg. Eight hours postpartum she suddenly collapsed and her blood pressure and pulse became unrecordable. Hydrocortisone 400 mg was given intravenously as a bolus and blood transfusion was started. During the next 2 hours she received 8 units of blood and the blood pressure rose to 120/110 mm Hg. She remained pale, with a persistent tachycardia of about 140/minute; the restlessness had decreased and the level of consciousness had improved. She complained of epigastric pain and a sensation of distension in the abdomen. Two hours later her blood pressure and pulse again became unrecordable. She was given a further 2 units of blood and 500 ml of Macrodex 70 and her blood pressure rose to 110/70 mm Hg. The radial pulse was barely palpable.

She was transferred to the Intensive Therapy Unit, Whipps Cross Hospital. On arrival she was pale and sweating; her pulse rate was 120/minute and her blood pressure 100/70 mm Hg. Her abdomen was grossly distended; no bowel sounds were audible. The abdominal distension was thought to be due to ileus related to her shocked condition. On vaginal examination the uterus was contracted and the cervical os closed. A central venous pressure line was set up and the reading recorded as +2 cm water. Despite vigorous intravenous therapy with whole blood and Macrodex 70 her central venous pressure repeatedly fell to zero and she remained severely shocked with cold clammy cyanosed extremities. The level of consciousness had deteriorated and the patient was oliguric. There was a persistent tachycardia of 120–180/minute and the blood pressure fluctuated between 120/110 mm Hg and a low unrecordable level. The abdomen became increasingly distended and 3 hours later shifting dullness was detected. Fresh blood was aspirated on a four-quadrant peritoneal tap. A surgical opinion was sought and an emergency laparotomy arranged.

At operation the peritoneal cavity was distended with blood which was found to be coming from the right lobe of the liver where the capsule had been completely stripped off and ruptured by a subcapsular haematoma. A large subcapsular haematoma was also found over the left lobe. Sheets of Sterispon were applied to the surface of the liver and omentum laid over it. A peritoneal dialysis catheter was positioned in the right iliac fossa.

Postoperatively the patient was transfused with fluid to maintain the central venous pressure at +4–10 cm water; the pulse remained at 120/minute. Her blood pressure was unrecordable for 12 hours and she remained anuric. Peritoneal dialysis was instituted.

Over the next 24 hours the blood pressure rose to 150/120 mm Hg and the dialysate, which was initially heavily blood-stained, began to clear. Intermittent intravenous diazoxide was required for 7 days in order to control the blood pressure. The patient was maintained on intermittent positive pressure ventilation for 10 days. During this time the level of consciousness steadily improved but her seriously ill condition necessitated gradual weaning off the ventilator.

Eleven days after admission a tracheostomy was performed which facilitated respiratory management. The tracheostomy tube was removed 10 days later.

Fourteen days postpartum, because of technical difficulties with peritoneal dialysis and the suspicion that dialysis might have to be continued for some time, haemodialysis was commenced. Seventeen haemodialyses were performed at Whipps Cross Hospital by the Mobile Renal Team. The patient was then transferred to the Renal Unit at the RAF Hospital, Halton, where haemodialysis was continued. She remained oliguric for 5 weeks. She was discharged home 3 weeks later. The creatinine clearance prior to discharge was 23 ml/minute.

Comment

This patient posed a difficult diagnostic problem. At first the collapse appeared to be due either to intrauterine haemorrhage or to septic shock. The former was excluded by vaginal examination and the latter was considered unlikely in the absence of an obvious source of sepsis. In view of the persistent tachycardia in the presence of an initial normal blood pressure (after volume replacement) and an associated decreased level of consciousness, the possibility of an overdose of chlormethiazole was considered.

It is interesting that when the blood pressure rose the pulse volume remained small and the diastolic pressure high; the high diastolic pressure was presumably related to pregnancy toxaemia and gave the misleading impression of a normal dynamic blood volume. It is evident that a diagnostic peritoneal tap should have been performed earlier. After surgery and replacement of the blood volume, the diastolic blood pressure over the next 7 days rose on several occasions to 110–120 mm Hg. This was unlikely to be due to fluid overloading since the central venous pressure remained normal and fluid balance was carefully controlled; it was probably related to postpartum toxaemia.

---

* C. H. Browne, G. C. Hanson and L. R. de Jode: Whipps Cross Hospital, Leytonstone, London. P. A. Roberts: Plaistow Maternity Hospital, Howards Road, London.

In view of the prolonged period of oliguria and the low creatinine clearance 2 months after the onset of renal failure, it is probable that this patient sustained partial renal cortical necrosis.

Discussion

Subcapsular haematoma of the liver and its rupture into the peritoneal cavity have been reported in several countries (Sheehan and Lynch, 1973) since its first description by Abercrombie (1844). Most of the case reports are from Central America, and there are very few from Britain (Roy, 1914; Bellwood, 1915; Links, 1946; Burton-Brown and Shepherd, 1949). Most of the cases were associated with toxaemia of pregnancy and some, as in our case, with eclampsia.

The characteristic hepatic lesion in toxaemia is haemorrhagic necrosis of the periphery of the hepatic lobule, especially of the right lobe. It seems likely that this haemorrhage beneath the liver capsule may extend, causing distension and rupture into the peritoneal cavity. Various factors have been suggested as contributing to the enlargement and rupture of the haematoma; these include slight trauma unrecognized by the patient (Barry and Meagher, 1964), contractions of the diaphragm and abdominal muscles associated with labour (Ayars et al., 1937) and hypertension with vomiting and convulsions (Speert and Tillman, 1952). Ninety-five per cent of hepatic haematomas occur over the anterior or superior surface of the right lobe; this would indicate that the causative factor was blunt trauma against the ribs. In the remaining patients the caudate lobe is involved adjacent to the vertebral column (Touloukian and Ferrer, 1967). In our case, however, the left lobe also contained a large subcapsular haematoma, but which had not ruptured the capsule.

Haematoma formation secondary to disseminated intravascular coagulation has been suggested (Pereyra and Lawler, 1956) as an aetiological factor. In our patient there was no haematological evidence of this.

Our patient complained of epigastric pain immediately postpartum and did not become shocked until after two eclamptic fits during which, presumably, the capsule ruptured.

The clinical picture of upper abdominal pain and gross shock without overt bleeding and in the face of vigorous intravenous replacement therapy should suggest this condition. Abdominal paracentesis provides relevant information for diagnosis (Mokotoff et al., 1967). Urgent laparotomy offers the only chance of survival. At operation various methods of achieving haemostasis have been advocated. These include packing the area with Surgicel (Touloukian and Ferrer, 1967), Sterispon, fat, muscle (Links, 1946) or omentum, suture with catgut on an atraumatic needle (Hakim-Elahi, 1965) and methyl alphacyanoacrylate (Just-Viera et al., 1962). Hepatic lobectomy has not been attempted. Adequate drainage is recommended. In our case the necessity for peritoneal dialysis in the face of acute renal failure enabled us to confirm that bleeding had stopped, as the dialysate became free of blood after 4 days.

The survival rate in operated cases is in the region of 50 per cent. Death usually results from failure to control the bleeding.

Acknowledgements

We thank Mrs R. Selby and Mrs J. Snell for their secretarial assistance, and also the Renal Team from the RAF Hospital, Halton, for their assistance in the management of this case.

References

ABERCROMBIE J. (1844) Case of haemorrhage of the liver. *Lond. Med. Gaz.* **34**, 792–794.

AYARS T. R., OHUM A. E. and CARLINGHOUSE R. E. (1937) Pregnancy with spontaneous subcapsular haematoma. *Weekly Bull. S. Louis. Med. Soc.* **25**, 311–312.

BARRY A. P. and MEAGHER D. J. (1964) Rupture of the liver complicating pregnancy. *J. Obstet. Gynecol.* **23**, 381–385.

BELLWOOD K. B. (1915) A fatal case of eclampsia. *St Barth. Hosp. J.* **22**, 154–155.

BURTON-BROWN J. R. C. and SHEPHERD J. A. (1949) Rupture of the liver associated with parturition. *Br. Med. J.* **1**, 941–943.

HAKIM-ELAHI E. (1965) Spontaneous rupture of the liver in pregnancy. *Obstet. Gynecol.* **26**, 435–439.

JUST-VIERA J. O., PURON-DEL AQUILLA R. and YEAGER G. H. (1962) Control of hemorrhage from the liver without use of sutures or clamps. *Am. Surg.* **28**, 754–758.

LINKS H. (1946) Spontaneous rupture of liver complicating pregnancy. *Br. Med. J.* **1**, 275–276.

MOKOTOFF R., WEISS L. S., BRANDON L. H. and CAMILEO M. F. (1967) Liver rupture complicating toxaemia of pregnancy. *Arch. Intern. Med.* **119**, 375–380.

PEREYRA A. J. and LAWLER M. P. (1956) Spontaneous rupture of the liver in afibrinogenemia during pregnancy. *Obstet. Gynecol.* **7**, 552–556.

ROY D. W. (1914) Purpural eclampsia; death due to rupture of subcapsular haematoma of the liver. *Proc. R. Soc. Med.* **8**, 13.

SHEEHAN H. L. and LYNCH J. B. (1973) *Pathology of Toxaemia of Pregnancy.* Edinburgh, Churchill Livingstone, p. 337.

SPEERT H. and TILLMAN A. J. B. (1952) Rupture of the liver in pregnancy. *Am. J. Obstet. Gynecol.* **63**, 1127–1130.

TOULOUKIAN R. J. and FERRER J. M. (1967) Rupture of the liver during pregnancy. *Am. Surg.* **33**, 432–436.

Br. J. Surg. Vol. 62 (1975) 239–242

Single layer anastomosis after rectosigmoid resection

N. A. MATHESON AND A. D. IRVING*

SUMMARY

Anastomosis after resection of the rectosigmoid colon is often followed by leakage at the suture line. When occult leakage discovered on routine contrast study is included incidence rates of over 50 per cent have recently been reported.

A single layer interrupted seromuscular inverting technique was used for the anastomosis after elective rectosigmoid resection in 52 consecutive patients. The total incidence of suture line leakage was 6 per cent. Therefore a high incidence of anastomotic dehiscence in the rectum can be avoided and it is concluded that a single layer technique is sound.

ANASTOMOSES after rectosigmoid resection appear to be prone to dehiscence, and the more thorough the search the more often is leakage found. In the experience of Goligher, Graham and de Dombal (1970) of 73 patients after anterior resection of the rectum, 40 per cent of anastomoses above the peritoneal reflection and 69 per cent of anastomoses below the peritoneal reflection showed leakage on contrast radiological study with barium about 14 days after operation. In most instances the degree of leakage was minor and not clinically apparent, but 4 of 47 patients after high rectal anastomosis (above the peritoneal reflection) and 7 of 26 after low rectal anastomosis (below the peritoneal reflection) developed either peritonitis or faecal fistula. In a recent comparison of continuous polyglycolic acid sutures with catgut for the all coats layer in two layer anastomoses of colon and colorectum, Clark et al. (1972) found radiological evidence of leakage in 2 of 6 patients after high anterior resection, and in 7 of 9 patients after low anterior resection, an overall incidence of 60 per cent. Of these 9 instances of leakage, 6 were clinically apparent.

For 12 years we have used a single layer of interrupted non-absorbable seromuscular sutures with inversion of mucosa in small bowel anastomosis, and for 6 years the same method has been used routinely in the colon and rectum. Fifty-two consecutive elective colorectal anastomoses made with such a technique were studied with regard to the incidence of leakage. All the patients were examined radiologically with Gastrografin enemas at about 10 days after operation, apart from 1 patient in whom leakage was clinically apparent. Leakage was found in 3 of the 52 patients (6 per cent) and was clinically apparent in 1 of the 3 (2 per cent). These results are an improvement on previously published series and are reported to encourage acceptance of a simple and safe method of anastomosis after rectosigmoid resection.

Patients and methods

During the past 6 years 52 patients have undergone elective resection of the rectosigmoid colon. The conditions requiring operation were carcinoma in 40, diverticular disease in 5 and miscellaneous conditions including stricture, volvulus, villous papilloma and endometriosis in 7. Except in the presence of obstruction, the bowel was mechanically prepared for 4 or 5 days using twice daily colonic lavage supplemented with magnesium sulphate by mouth until there was diarrhoea. During this time phthalylsulphathiazole 4 g daily was given, but other antibiotics were not used.

In the presence of obstruction sufficient to interfere with efficient cleansing of the colon a preliminary transverse colostomy was made, and this was done in 11 patients. A colostomy was made at the time of resection in only 1 patient. Of the 52 operations, the anastomosis was above the peritoneal reflection in 29, at or about the level of the reflection in 8 and below the reflection in 15. Anastomoses at or above the reflection were classified as 'high' and below the reflection as 'low' (Goligher, Graham and de Dombal, 1970); there were therefore 37 high and 15 low anastomoses.

In resection for carcinoma, division of the inferior mesenteric artery and vein was either at the level of the origin of the artery or more usually immediately below the left colic branch. In carcinoma the rectal stump was washed out with 1 : 500 mercuric perchloride and the proximal bowel end was cleansed with a similar solution. Clamps were applied only to the segment of bowel to be resected. The sutures for each operation were made up in anastomosis packets containing 24, 16-mm half circle fine needles threaded with either 40-cm or 75-cm lengths of 2/0 braided nylon (Arbralon, Armour Pharmaceuticals Co. Ltd), depending on the depth of the proposed anastomosis. The posterior layer of seromuscular sutures was inserted parallel to the long axis of the bowel (except for those at each end which were placed first horizontally) at intervals of approximately 5 mm. The proximal bowel was then slid down to the rectal stump and the sutures tied and cut. The anterior layer was made in a similar way, the sutures being tied and cut after the complete series had been inserted.

For many years, if there was pelvic sepsis or obvious faecal contamination at operation, we have washed out the pelvis with 1 litre of saline containing 1 g tetracycline. During the past 2 years this has become routine after colorectal anastomosis.

---

* Department of Surgery, University of Aberdeen and Aberdeen Royal Infirmary.

A drain was used in 26 of the 37 high anastomoses and in all the low anastomoses. The pelvis was not 'reperitonealized'.

The use of neostigmine to reverse the effects of relaxant drugs was avoided since this may contribute to anastomotic dehiscence (Bell and Lewis, 1968) and we are uncertain that giving atropine beforehand completely abolishes the effect of neostigmine on the gut.

All anastomoses were studied radiographically using Gastrografin at or about 10 days after operation, except in 1 patient in whom there was clear clinical evidence of dehiscence.

Table I: SUMMARY OF THE RESULTS

Type of anastomosis	No. of anastomoses	Clinical leak	Radiological leak	Total No.	Total %
High	37	1	1	2	5
Low	15	0	1	1	7
Total	52	1	2	3	6

Results

The results are summarized in *Table I.*

Brief details of the 3 patients in whom anastomotic leakage occurred are given below.

Case 1: A 63-year-old female was operated on electively for carcinoma of the sigmoid colon. There was a fistula between the carcinoma and the jejunum and an extensive associated pelvic abscess, extending to affect the anterior abdominal wall. The carcinoma was resected together with a length of jejunum and the anastomosis was above the peritoneal reflection. A colostomy was not made. There was wound disruption with extensive abdominal wall sepsis early after operation, followed by clinical evidence of leakage at 10 days with a faecal discharge and lower abdominal peritonitis. Re-exploration showed a leak just distal to the anastomosis. The bowel ends were exteriorized, but the patient died of continuing sepsis 1 week later.

This instance of leakage is, strictly speaking, not anastomotic, but the distinction is fine and we feel it right to include the patient as such.

Case 2: A 77-year-old male underwent elective resection for carcinoma of the sigmoid colon. The anastomosis was above the level of the peritoneal reflection. At routine Gastrografin enema examination free leakage of contrast was seen, but this was never clinically apparent.

Case 3: A 74-year-old female underwent elective resection for rectal carcinoma, with the anastomosis well below the level of the peritoneal reflection. Routine Gastrografin enema examination showed free leakage of contrast but this was never clinically apparent.

Of the 3 instances of leakage 1 was gross and clinically apparent, whereas 2 were occult, demonstrable only on the contrast study, and evidently did not interfere with the patient's clinical course. Two leaks (1 gross and 1 occult) occurred in 37 high rectal anastomoses (5 per cent) and 1 occult leak occurred in 15 low anastomoses (7 per cent). Dehiscence was not seen in any of the 11 patients with a preliminary colostomy or in the patient with a simultaneous colostomy.

Discussion

Because of the morbidity and mortality (Goligher, Graham and de Dombal, 1970, Schrock et al., 1973), breakdown of anastomoses in the colon and rectum is a topic of serious surgical concern. Particular attention is focused on the rectum where anastomosis is evidently associated with an incidence of dehiscence in excess of that elsewhere in the intestine.

Conditions affecting the healing of large bowel anastomoses have been reviewed by Hunt and Hawley (1967), Goligher, Graham and de Dombal (1970), Rosenberg et al. (1971), Hawley (1973), Irvin and Goligher (1973) and Schrock et al. (1973). These include general factors such as age, nutritional status, the use of steroids, the nature of the underlying disease and blood loss requiring transfusion.

Efficient bowel preparation (Rosenberg et al., 1971) and the use of an inverting anastomotic technique (Goligher, Morris et al., 1970; McAdams et al., 1970; Irvin and Edwards, 1973) contribute to safety, whereas local sepsis or faecal soiling leads to increased breakdown rates (Letwin et al., 1967; Hawley, 1970; Rosenberg et al., 1971; Debas and Thomson, 1972).

The unwisdom of attempting primary colorectal anastomosis under adverse local conditions is exemplified by the patient in the present series who developed clinically obvious leakage, and additionally by our experience with 2 patients who underwent emergency anterior resection with primary anastomosis during the past 5 years, one a palliative resection in the presence of obstruction with faecal loading and the other resection for perforated diverticular disease with gross pelvic sepsis. Both patients developed clinically obvious leakage and the first died from peritonitis.

A 'protective' colostomy made at the time of resection and anastomosis does not appear to affect the incidence of dehiscence although it may reduce ensuing mortality and morbidity (Goligher, Graham and de Dombal, 1970; Schrock et al., 1973). Such a colostomy was made in only 1 patient in the present series and therefore did not influence the results. However, a preliminary colostomy was made if associated obstruction was thought sufficient to interfere with thorough mechanical preparation, and this was done in 11 patients.

A single layer method of intestinal anastomosis was first advised by Halsted in 1887 and was routinely used by Wilkie (1934). Wangensteen (1945) advocated a single layer technique when he described conservative resection for carcinoma of the rectum, and Gambee et al. (1956), describing results of their experience with single layer techniques over 10 years, reported 163 colonic anastomoses with 11 leaks. The method, however, has never gained orthodoxy in the United Kingdom and Aird's (1957) comment that it requires 'a confidence and courage that most of us lack' may be apt.

Single layer inverting methods have been shown experimentally to be superior to two layer inverting techniques with respect to luminal reduction (Halsted, 1887; Letwin et al., 1967; Orr, 1969; McAdams et al., 1970), tissue strangulation (Letwin et al., 1967; Orr, 1969) and anastomotic strength after the fifth postoperative day (Hamilton, 1967; Letwin et al., 1967; Orr, 1969; McAdams et al., 1970). Histologically, mucosal continuity and muscle realignment occur more rapidly with single layer methods (Orr, 1969; McAdams et al., 1970), and angiographically, healing may be more rapid (Orr, 1969) although this has been disputed (Abramowitz and McAlister, 1969).

There is therefore a great deal of experimental evidence in favour of single layer anastomosis, although not all authors have been able to confirm its superiority in reducing mortality or anastomotic complications (McAdams et al., 1970; Irvin and Edwards, 1973).

The clinical use of single layer methods in rectal anastomosis has seldom been reported, and some American series deliberately exclude this area. A randomized clinical trial (Irvin et al., 1973) comparing single layer with two layer inverting anastomosis in the small and large bowel showed a similar incidence of leakage with each method. Only 7 patients in each group underwent rectal anastomosis, with 2 instances of dehiscence in the two layer group and 1 in the single layer group. A conclusion with specific regard to the rectum cannot therefore be made. A relatively high incidence of dehiscence after single layer anastomosis elsewhere in the intestine is surprising. Whether this is related to the fact that different types of single layer technique were used, that various surgeons were involved and that they were presumably unaccustomed to single layer anastomosis is uncertain but possible.

The reported incidence of leakage in patients undergoing elective resection with conventional two layer colorectal anastomosis and studied radiographically after operation has been 51 per cent (Goligher, Graham and de Dombal, 1970) and 60 per cent (Clark et al., 1972). Further, when the anastomosis was low the incidence of leakage was substantially higher. It is unlikely that either our patients or their management were fundamentally different from those in earlier reports and we are therefore inclined to attribute the low incidence of leakage (6 per cent overall; 7 per cent in low anastomoses) to the single layer anastomotic technique described here. Apart from the safety associated with the use of a single layer technique, there are other advantages of which the most appealing is simplicity. This is especially apparent in very low rectal anastomoses; it is half as difficult to insert one layer of sutures in a deep confined space as it is to insert two. An associated feature is therefore expedience. A less apparent advantage which may nevertheless be significant is that a single layer seromuscular technique avoids mucosal puncture and in theory should be associated with less risk of malignant cell implantation in patients with large bowel carcinoma.

Acknowledgement
We are indebted to Professor H. A. F. Dudley who introduced us to single layer techniques and we thank Dr R. G. Mahaffy for carrying out the Gastrografin studies.

References

ABRAMOWITZ H. B. and MCALISTER W. H. (1969) A comparative study of small bowel anastomoses by angiography and microangiography. *Surgery* **66**, 564–569.

AIRD I. (1957) *A Companion in Surgical Studies*, 2nd ed. Edinburgh, Livingstone, p. 891.

BELL C. M. A. and LEWIS C. B. (1968) Effect of neostigmine on integrity of ileorectal anastomoses. *Br. Med. J.* **3**, 587–588.

CLARK C. G., ELMASRI S., HARRIS J., WYLLIE J. H. and DOW J. (1972) Polyglycolic-acid sutures and catgut in colonic anastomoses, a controlled clinical trial. *Lancet* **2**, 1006–1007.

DEBAS H. T. and THOMSON F. B. (1972) A critical review of colectomy with anastomosis. *Surg. Gynecol. Obstet.* **135**, 747–752.

GAMBEE L. P., GARNJOBST W. and HARDWICK C. E. (1956) Ten years' experience with a single layer anastomosis in colon surgery. *Am. J. Surg.* **92**, 222–227.

GOLIGHER J. C., GRAHAM N. G. and DE DOMBAL F. T. (1970) Anastomotic dehiscence after anterior resection of rectum and sigmoid. *Br. J. Surg.* **57**, 109–118.

GOLIGHER J. C., MORRIS C., MCADAM W. A. F., DE DOMBAL F. T. and JOHNSTON D. (1970) A controlled trial of inverting versus everting intestinal suture in clinical large bowel surgery. *Br. J. Surg.* **57**, 817–822.

HALSTED W. S. (1887) Circular suture of the intestine—an experimental study. *Am. J. Med. Sci.* **94**, 436–461.

HAMILTON J. E. (1967) Reappraisal of open intestinal anastomoses. *Ann. Surg.* **165**, 917–923.

HAWLEY P. R. (1970) Infection—the cause of anastomotic breakdown; an experimental study. *Proc. R. Soc. Med.* **63**, 752.

HAWLEY P. R. (1973) Causes and prevention of colonic anastomotic breakdown. *Dis. Colon Rectum* **16**, 272–277.

HUNT T. K. and HAWLEY P. R. (1967) Surgical judgement and colonic anastomoses. *Dis. Colon Rectum* **12**, 167–171.

IRVIN T. T. and EDWARDS J. P. (1973) Comparison of single layer inverting, two layer inverting and everting anastomoses in the rabbit colon. *Br. J. Surg.* **60**, 453–457.

IRVIN T. T. and GOLIGHER J. C. (1973) Aetiology of disruption of intestinal anastomoses. *Br. J. Surg.* **60**, 461–464.

IRVIN T. T., GOLIGHER J. C. and JOHNSTON D. (1973) A randomized prospective clinical trial of single layer and two layer inverting intestinal anastomoses. *Br. J. Surg.* **60**, 457–460.

LETWIN E., WILLIAMS H. T. G. and HARRISON R. C. (1967) The experimental healing of soft tissues. *J. R. Coll. Surg. Edinb.* **12**, 121–132.

MCADAMS A. J., MEIKLE A. G. and TAYLOR J. O. (1970) One layer or two layer colonic anastomoses? *Am. J. Surg.* **120**, 546–550.

ORR N. W. M. (1969) A single layer intestinal anastomosis. *Br. J. Surg.* **56**, 771–774.

ROSENBERG I. L., GRAHAM N. G., DE DOMBAL F. T. and GOLIGHER J. C. (1971) Preparation of the intestine in patients undergoing major large bowel surgery, mainly for neoplasms of the colon and rectum. *Br. J. Surg.* **58**, 266–269.

SCHROCK T. R., DEVENEY C. W. and DUNPHY J. E. (1973) Factors contributing to leakage of colonic anastomoses. *Ann. Surg.* **177**, 513–518.

WANGENSTEEN O. H. (1945) Primary resection (closed anastomosis) of rectal ampulla for malignancy with preservation of sphincteric function. *Surg. Gynecol. Obstet.* **81**, 1–23.

WILKIE D. P. D. (1934) Cancer of the colon. Its surgical treatment. *Lancet* **1**, 65–68.

Br. J. Surg. Vol. 62 (1975) 243–245

Temporary transcaecal ileal diversion in prevention of anastomotic leak in planned colonic surgery (an alternative to proximal colostomy)

ALAN SIMPSON AND V. K. SRIVASTAVA*

SUMMARY

An alternative to proximal colostomy in planned colonic resection is reported in 30 patients. The physiopathological background for this procedure of temporary transcaecal ileal diversion is explained together with details of the operation and the results obtained.

ANASTOMOTIC leakage after colonic surgery is a hazardous complication, responsible for considerable morbidity and mortality. The immediate success in this field of surgery is almost entirely dictated by the absolute integrity of the anastomosis. At the turn of the century the mortality from this complication alone was between 30 and 50 per cent (Beahrs, 1967).

The recognition of the importance of the influence of leakage from the anastomosis on the immediate morbidity and mortality led to the development of temporary proximal faecal diversion techniques to protect the anastomotic site. These diversions, such as proximal colostomy, caecostomy, etc., have gone a long way towards minimizing the risk of leakage from the anastomosis in colonic resections. However, recent doubt have been cast on the efficacy of such procedures as shown by Irvin and Goligher (1973) and also in our control series.

It appears from the recent literature that not only is the risk of leakage still high (varying from 16 to 51 per cent, the highest incidence being in anterior resections of rectum) but the morbidity and resulting mortality are also appreciable (Herter and Slanetz, 1967; Goligher et al., 1970; Whitaker et al., 1970).

Frequently faced with this problem of colonic anastomosis and appreciating the disadvantages of adding a proximal diversion in planned colonic resections, we considered that the solution lay in finding a diversion technique which could be a part of a one-stage procedure, thereby avoiding the problems associated with the colostomy and its subsequent closure. In our opinion an effective proximal diversion must provide complete physiological and mechanical rest to the anastomosis; this is essential for the healing at the anastomosis to progress unhindered to completion, the anastomosis only regaining its leakproof conducting capacity when healing has been allowed to progress unhindered to completion. In our experience this is not achieved by proximal colostomy (as explained later).

A new technique designed to achieve temporary total proximal diversion has been successfully used in 30 cases of planned colonic resections and is described below.

Patients

The series consisted of 133 planned colonic resections with either colocolic or colorectal anastomosis performed in the West Bromwich Group of Hospitals. One hundred and three cases (control group) were chosen by random selection from cases operated upon by three surgical teams between 1966 and 1974. The remaining 30 patients had the new diversion technique incorporated at the time of resection (1970–4). The control group of 103 cases is compared with these 30 cases for the incidence of anastomotic leakage only.

Methods

Faecal leakage in the present series of cases was evidenced by either the occurrence of faecal peritonitis and/or the appearance of a faecal fistula. Cases with subclinical leakage obviously could not be included.

Clinically, the leakage was divided into major and minor. A major leak meant either faecal peritonitis or persistent faecal fistula. A minor leak included those anastomoses which healed with conservative treatment, without markedly hindering the clinical recovery of the patient.

All the cases including the control series had an intraperitoneal drain to the anastomosis.

Techniques

All the 30 patients had resection of the colon with a two layer anastomosis, the outer layer being interrupted unabsorbable sutures. The technique and level of resection were dictated by the nature and site of the lesion. Unloading of the colon proximal to the resection was ensured as far as possible in every case. After the completion of the resection and anastomosis in the 30 patients, a temporary total ileal-transcaecal diversion was carried out as described below. Appendicectomy was performed and a purse string suture was placed around the base of the appendix site. (If appendicectomy had been performed previously, then a small incision was made in the caecal wall and a similar purse string suture was placed around it.) Via this lumen (appendix base or caecostomy incision) a 22 or 24 French gauge soft Foley-type inflatable catheter was negotiated through the ileocaecal valve into the terminal ileum for a distance of at least

---

* Sandwell Area Health Authority Hospitals, Staffordshire.

Br. J. Surg. Vol. 62 (1975) 243–245

Temporary transcaecal ileal diversion in prevention of anastomotic leak in planned colonic surgery (an alternative to proximal colostomy)

ALAN SIMPSON AND V. K. SRIVASTAVA*

SUMMARY

An alternative to proximal colostomy in planned colonic resection is reported in 30 patients. The physiopathological background for this procedure of temporary transcaecal ileal diversion is explained together with details of the operation and the results obtained.

ANASTOMOTIC leakage after colonic surgery is a hazardous complication, responsible for considerable morbidity and mortality. The immediate success in this field of surgery is almost entirely dictated by the absolute integrity of the anastomosis. At the turn of the century the mortality from this complication alone was between 30 and 50 per cent (Beahrs, 1967).

The recognition of the importance of the influence of leakage from the anastomosis on the immediate morbidity and mortality led to the development of temporary proximal faecal diversion techniques to protect the anastomotic site. These diversions, such as proximal colostomy, caecostomy, etc., have gone a long way towards minimizing the risk of leakage from the anastomosis in colonic resections. However, recent doubt have been cast on the efficacy of such procedures as shown by Irvin and Goligher (1973) and also in our control series.

It appears from the recent literature that not only is the risk of leakage still high (varying from 16 to 51 per cent, the highest incidence being in anterior resections of rectum) but the morbidity and resulting mortality are also appreciable (Herter and Slanetz, 1967; Goligher et al., 1970; Whitaker et al., 1970).

Frequently faced with this problem of colonic anastomosis and appreciating the disadvantages of adding a proximal diversion in planned colonic resections, we considered that the solution lay in finding a diversion technique which could be a part of a one-stage procedure, thereby avoiding the problems associated with the colostomy and its subsequent closure. In our opinion an effective proximal diversion must provide complete physiological and mechanical rest to the anastomosis; this is essential for the healing at the anastomosis to progress unhindered to completion, the anastomosis only regaining its leakproof conducting capacity when healing has been allowed to progress unhindered to completion. In our experience this is not achieved by proximal colostomy (as explained later).

A new technique designed to achieve temporary total proximal diversion has been successfully used in 30 cases of planned colonic resections and is described below.

Patients

The series consisted of 133 planned colonic resections with either colocolic or colorectal anastomosis performed in the West Bromwich Group of Hospitals. One hundred and three cases (control group) were chosen by random selection from cases operated upon by three surgical teams between 1966 and 1974. The remaining 30 patients had the new diversion technique incorporated at the time of resection (1970–4). The control group of 103 cases is compared with these 30 cases for the incidence of anastomotic leakage only.

Methods

Faecal leakage in the present series of cases was evidenced by either the occurrence of faecal peritonitis and/or the appearance of a faecal fistula. Cases with subclinical leakage obviously could not be included.

Clinically, the leakage was divided into major and minor. A major leak meant either faecal peritonitis or persistent faecal fistula. A minor leak included those anastomoses which healed with conservative treatment, without markedly hindering the clinical recovery of the patient.

All the cases including the control series had an intraperitoneal drain to the anastomosis.

Techniques

All the 30 patients had resection of the colon with a two layer anastomosis, the outer layer being interrupted unabsorbable sutures. The technique and level of resection were dictated by the nature and site of the lesion. Unloading of the colon proximal to the resection was ensured as far as possible in every case. After the completion of the resection and anastomosis in the 30 patients, a temporary total ileal-transcaecal diversion was carried out as described below. Appendicectomy was performed and a purse string suture was placed around the base of the appendix site. (If appendicectomy had been performed previously, then a small incision was made in the caecal wall and a similar purse string suture was placed around it.) Via this lumen (appendix base or caecostomy incision) a 22 or 24 French gauge soft Foley-type inflatable catheter was negotiated through the ileocaecal valve into the terminal ileum for a distance of at least

---

* Sandwell Area Health Authority Hospitals, Staffordshire.

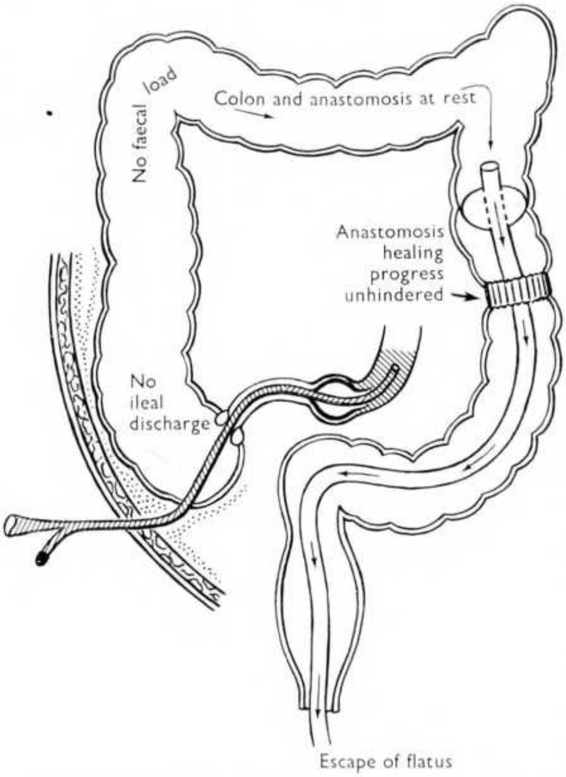

No faecal load
Colon and anastomosis at rest
Anastomosis healing progress unhindered
No ileal discharge
Escape of flatus

Fig. 1. Diagram of the completed colonic resection with total ileal diversion.

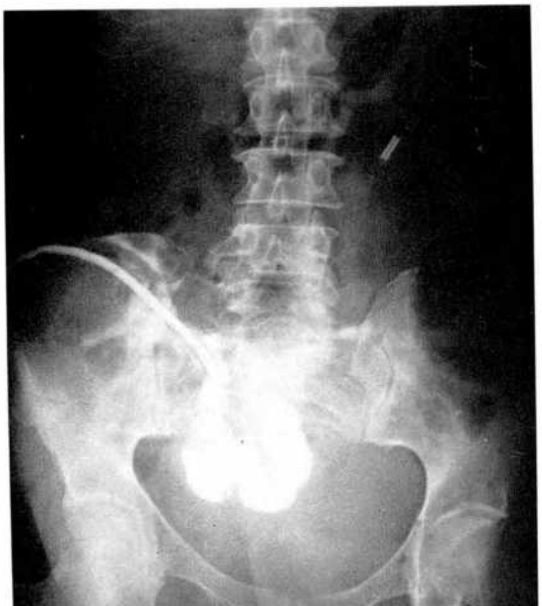


Fig. 2. X-ray film showing the catheter in position and unobstructed flow of contrast media after deflation of the balloon.

15 cm beyond the ileocaecal junction (this tube had been previously brought through an incision in the anterior abdominal wall in the right iliac fossa).

The patency of the lumen and the competence of the balloon of the catheter having been checked beforehand, the balloon was inflated inside the terminal ileum just sufficiently to occlude the lumen of the ileum without causing ischaemia or undue pressure on the ileal wall. The purse string suture around the catheter in the caecal wall was then tightened and the caecostomy site was sutured to the lateral wall of the peritoneum so as to make a leakproof seal between the caecum and anterior abdominal wall.

In some cases of low left colonic resection the anastomosis was also intubated by a rectal tube or large size balloon catheter brought out through the anus; this was left in position for the first 48 hours (*Fig.* 1). Finally, the site of the anastomosis was drained by the use of a corrugated drain.

Postoperative care

In addition to the standard postoperative management particular attention was paid to the following points:

1. Maintenance of patency of the pathway of the catheter into the ileum, this being ensured by occasional injection of 10–15 ml of sterile water or saline (by bladder wash syringe) into the catheter to make sure the channel was clear. This was done once or twice daily as required.
2. A gradual deflation of the balloon of the catheter, beginning on the second postoperative day, was carried out, so that the balloon would be completely deflated by about the sixth or the seventh day; this would allow a gradual flow of the ileal contents into the colon.
3. Careful note of the volume of ileal discharge per day to ensure the catheter bulb was not obstructing the ileum.
4. A radiographic study was done in some cases by injecting Gastrografin into the ileum via the ileal diversion catheter, to see any adverse effect. *Fig.* 2 shows the catheter in position and unobstructed flow of the contrast after partial deflation of the balloon.

Physiopathological basis underlying the operation of temporary transcaecal ileal diversion in colonic resection

The colon is a neuromuscular tube whose main function is to hold and transmit faeces. This is ensured by its reservoir capacity and its ability to carry out controlled segmental and mass peristaltic movements. Any resection (or section) of this neuromuscular tube must interfere with the function of transmission at the point of transection. The restoration of physiological continuity is not immediately obtained by achieving a physical continuity (anastomosis) by means of sutures. Effective leakproof transmitting capabilities are only regained after the natural healing processes have completely sealed the gap. We postulate that in the early stages of healing the anastomotic site presents, to a lesser or greater extent, a ring of obstruction due not to narrowing or physical constriction but to a

However, if the obstruction is due to diverticular disease the ureter should be preserved as recovery is likely after the resection of the diverticular mass. Therefore it is important to make a diagnosis preoperatively, and colonoscopy (Williams and Teague, 1973) together with silicone foam enema (Cook and Margulis, 1961; Hughes, 1969) may be helpful in the difficult case in addition to the routine sigmoidoscopy and barium enema examination. Nevertheless where doubt remains the treatment of a mass of dubious pathology in the sigmoid colon is resection, so that a diagnosis may be established and adequate treatment be performed.

Acknowledgements
We wish to thank Mr R. Williams, FRCS, for permission to publish details of his patient, and Professor L. E. Hughes for his advice and criticism.

References

BOLT D. E. and HUGHES L. E. (1966) Diverticulitis: a follow up of 100 cases. *Br. Med. J.* **1**, 1205–1209.

COLCOCK B. P. and SASS R. E. (1954) Diverticulitis and carcinoma of the colon: differential diagnosis. *Surg. Gynecol. Obstet.* **99**, 627–633.

COLCOCK B. P. and STAHMANN F. D. (1972) Fistulas complicating diverticular disease of the sigmoid colon. *Ann. Surg.* **175**, 838–846.

COOK G. B. and MARGULIS A. R. (1961) The silicone-foam diagnostic enema. 1. An assessment with surgical specimens of human sigmoid colon. *Surgery* **50**, 513–518.

GOW J. G. (1972) An appraisal of inflammatory stricture of the ureter. *Ann. R. Coll. Surg. Engl.* **51**, 177–189.

GOW J. G. (1974) Personal communication.

HARLIN H. C. and HAMM F. C. (1952) Urological disease resulting from non-specific inflammatory conditions of the bowel. *J. Urol.* **68**, 383–392.

HUGHES L. E. (1969) The use of the polysiloxane foam enema as a diagnostic tool for the left colon. In: *Detection of Colon Lesions. First Standardisation Conference* (American College of Radiology Ad Hoc Committee on the Detection of Cancer of the Colon). American College of Radiology, pp. 177–182.

LETT SIR H. (1932) Discussion of urinary complications of diseases of large intestine. *Proc. R. Soc. Med.* **25**, 1811.

MADSEN C. M. and THYBO E. (1972) Urological complications in diverticulitis of the sigmoid colon. *Acta Chir. Scand.* **138**, 207–210.

MAYO C. W. and BLUNT C. P. (1950) Vesico-sigmoidal fistulas complicating diverticulitis. *Surg. Gynecol. Obstet.* **91**, 612–616.

PONKA J. L., FOX J. DE W. and BRUSH B. E. (1959) Co-existing carcinoma and diverticula of the colon. *Arch. Surg.* **79**, 373–384.

RODKEY G. V. and WELCH C. E. (1965) In: Diverticulitis of the colon: evolution in concept and therapy. *Surg. Clin. North Am.* **45**, 1231.

WILLIAMS C. and TEAGUE R. H. (1973) Colonoscopy. *Gut* **14**, 990–1003.

Br. J. Surg. Vol. 62 (1975) 250–252

Reviews and notices of books

Progress in Pediatric Surgery. Volume 7
Edited P. P. Rickham, W. Ch. Hecker, and J. Prevot 230×155 mm. Pp. 170. Illustrated. 1974. Munich: Urban & Schwarzenberg. No price given.

THIS is the seventh volume of a new occasional book on paediatric surgery. It is difficult to differentiate it from yet another journal except in its excellent binding. The book contains nine different papers, and only three of these, dealing with reflux oesophagitis, are related to each other. The first paper on stenosis of the oesophagus secondary to hypopharyngeal abscess in the newborn is interesting and reports in detail 5 patients who were all cured. The second paper deals with unusual Siamese twins, the separation attempt leading to the death of both twins. Other papers deal with embryonic sarcomata, congenital duplication of the alimentary tract, obstructive valves of the posterior urethra and primary hepatic tumours in infancy and childhood. All the papers are extremely good and the book is recommended to all those practising paediatric surgery.

H. B. ECKSTEIN

Surgery of the Gastrointestinal Tract
Edited by John S. Najarian, MD, and John P. Delaney, MD. 235×160 mm. Pp. 320+xiv. Illustrated. 1973. New York: Symposium Specialists. $17.50.

IF you like 'reading surgery' in bed, then this is the ideal bedside book. It is composed of about fifty contributions on a multitude of topics, both practical and theoretical, by numerous well-known authorities. They are taken from the proceedings of the Continuation Course on Surgery of the Gastrointestinal Tract organized by the University of Minnesota Department of Surgery. It is impossible to list all the subjects and it would be invidious to mention only some of the authors. Suffice it to say that anyone who operates on the alimentary tract from the oesophagus down will find much of interest. The book is a delightful mix of scientific observation and clinical experience, orthodox and unusual ideas on surgical treatment, surgical technique and experimental studies. All in all, it is an excellent and enjoyable collection of essays by surgeons for surgeons to dip into in a spare moment or even when seeking advice on a difficult clinical problem.

ALAN G. COX.

Mammary Cancer and Neuroendocrine Therapy
Edited Basil A. Stoll, London. 220×160 mm. Pp. 421+xi. Illustrated. 1974. London: The Butterworth Group. £7·50.

To do this book justice would require the reviewer to be as erudite as the editor is in his field. Few can be and this reviewer certainly is not. Nevertheless this book can be recommended strongly, for it brings together a thoroughly confusing and often clinically agonizing subject in a way that provides an up-to-date reference source. It is not, nor does it set out to be, a primer of management for the patient with advanced breast cancer. Rather it is a background of biological information to which the clinician can turn in an endeavour to explain and rationalize the behaviour of his patients. The editor's own contribution is massive and extends also to the text, which is of a high standard and without many of the jerks and humps that characterize multiple authorship.

It is a pity that this symposium, generated, one is glad to see, without the expense of bringing people together, will be rendered out of date so quickly by the advancing tide of facts. Nevertheless, it is a lighthouse for the moment and should be sought out wherever two or three are gathered together trying to help patients with curable and incurable malignancy of the breast.

H. A. F. DUDLEY

Progress in Paediatric Neurosurgery
Edited K. A. Bushe, Göttingen, O. Spoerri, Göttingen, and J. Shaw, Edinburgh. 270×185 mm. Pp. 320, with 268 illustrations. 1974. Stuttgart: Hippokrates Verlag. DM.158.

THIS volume contains the text of 103 papers read at the third European Congress of Paediatric Neurosurgery in September 1972. There has been very little editing, which is doubtless one reason why publication has been possible less than 2 years after the congress. The result is a miscellaneous collection of short papers of uneven quality, many of which, however, will prove of interest to paediatric neurosurgeons, paediatricians, neurologists, neuroradiologists and others who take part in the management of childhood diseases affecting the central nervous system. Almost every reader will find papers of particular importance in his own field of work, especially in the review papers such as those on tumours of the cerebral hemispheres, on intrasellar and suprasellar tumours and on spinal tumours; many of these are by authors who can call upon considerable personal experience.

There are useful collections of papers on subdural effusions and on hydrocephalus with spina bifida aperta. These serve well to remind the reader of the great variation in concepts, methods of treatment and results which are possible in the rapidly developing field of paediatric neurosurgery.

Although the editors clearly did not wish to alter the papers (which range from the concise and formal to the wastefully discursive and conversational style) they should have exercised control of the references. One paper is only a little longer than its references while others contain none at all.

The publishers have clearly found that there is sufficient demand for volumes such as this one which serve to record the proceedings of congresses, but in this age when few of us can keep abreast with the literature in our own subject, a more rigid selection, or, better, publication of worthy papers in the regular journals, should be sufficient. Despite these strictures, these pages contain much valuable information for which neurosurgeons and others will be grateful.

KENNETH TILL

Principles and Practice of Modern Surgery
A. L. Som, Calcutta. Third edition. 245×195 mm. Pp. 172+xii, with 1050 illustrations. 1974. Calcutta: Sadhana Press. No price given.

IT is an indication of its popularity that this is the third edition of a work that first appeared as recently as 1961. In both the second and the present editions the text has been extensively revised. This together with the original production is a tribute to the erudition and the industry of the author.

There are those in Britain who think that much has been lost by the swing away from the teaching of the principles and practice of surgery. The content of this book suggests that its author has no such inhibition. First and foremost, Professor Asita Lal Som is a generalist and his purpose is to inform his readers about surgery; what surgery has to offer, what choice of procedure is available for the relief of many and various conditions and how each operation is carried out, step by step. Pathology and diagnosis are covered and a fair amount of basic surgical and theatre technique is included.

The first eleven chapters are devoted to general pathology; the remaining forty-six to vascular, abdominal, orthopaedic, urological, hormonal, plastic, dental, laryngological, mammary, oesophageal, thoracic and cardiac surgery and to the central and peripheral nervous systems, with, for good measure, sections on dental conditions, the face, head and neck, organ transplantation and reconstructive vascular surgery. There are many illustrations—some ingenious, many good and helpful, a few not so good.

Only dogmatic teaching and a laudable economy of word and phrase have made it possible to put all this between boards. The paper and printing are impeccable. That there are typographical errors is inevitable. That there are some expressions of opinion and even some statements of fact with which the reviewer would disagree is, in such a work, pardonable. Overall, in an age in which undergraduate teaching in Britain has become so academic, it is refreshing to find Asita Lal Som, as he certainly does, 'informing' his students 'about surgery'.

CHARLES WELLS

Machine Diagnosis and Information Retrieval in Medicine in the USSR

Edited A. A. Vischnevskiy, I. I. Artobolevskiy and M. L. Bykhovskiy. 232×150 mm. Pp. 138+viii. Illustrated. 1973. US Department of Health, Education and Welfare. No price given.

THE only excuse for reviewing this book in the BRITISH JOURNAL OF SURGERY is that the surgical decision-making situation has provided the model for some of the most productive studies in diagnostic process. The work of de Dombal's group in Leeds is an outstanding example and has exemplified what this book does not—the need to keep studies of decision-making realistic and in touch with what a clinician is doing day by day. Of course we are looking at a series of papers brought together as a monograph 5 years ago, and furthermore at work which was intended mainly to give a theoretical and mathematical frame against which decision making could be studied. Nevertheless, it is a little disappointing not to see more in the way of results. Those quoted on jaundice are not all that impressive, but doubtless, as in this country and the United States, the later figures are better.

The monograph also illustrates the big gap that still exists between clinicians and mathematicians. A good deal of the jargon and some of the mathematical manipulation is unintelligible unless one is familiar with the work at a research level. It is a pity that those who attack the problem from the analytical end do not spend more time on logical explanation and less on the intricacies of mathematics. What is badly needed is an up-to-date book on new pathways in the analysis of diagnostic process written by a clinician, preferably of course a surgeon. Meanwhile any text is welcome such as this which provides—to paraphrase Henry James—a particular insight from the position in which it stands.

H. A. F. DUDLEY

Instructional Course Lectures. Volume XXII, 1973

The American Academy of Orthopaedic Surgeons. 285×220 mm. Pp. 322+x. Illustrated. 1973. London: Henry Kimpton. £11·20.

THIS volume is a selection of lectures given at the Instructional Courses of the American Academy of Orthopaedic Surgeons; in addition, there is a superb review article on fat embolism by Beck and Collins which could be read with profit by those responsible for the management of major trauma. The clinical aspects, pathology and theories of causation are discussed in detail and there is a critical and stimulating approach to treatment.

Some of the other contributions are almost of the same quality and the editorial committee is to be congratulated on producing one of the best volumes in the series. The article by Connolly and Brooks on vascular problems in orthopaedics is first class; it gives a clear and concise account of the effect of ischaemia on nerve and muscle and emphasizes the importance of fasciotomy in addition to repair of the damaged artery in the management. Swanson describes arthritic disorders of the thumb and the place of flexible implant arthroplasties in the treatment.

The chapter on fractures and dislocations of the hip contains much good advice, which is marred by a recommendation by Lowell that immediate arthroplasty should be considered for bursting fractures of the acetabulum when it is not possible to achieve a stable reduction or a congruous relationship between the femoral head and acetabulum; surely it would be wiser to reserve arthroplasty for patients who are left with appreciable disability.

There is an excellent article by Rhinelander on the effects of medullary nailing on the blood supply of cortical bone. Some of the contributors to this chapter are too liberal with their indications for this technique and readers should digest the section by Brewer on the errors and complications before accepting their advice.

The chapter on Perthes's disease is in places repetitive. The natural history is well described by Fisher; the indications and results of conservative treatment and innominate osteotomy are clearly stated by Gosling and Salter. Urist writes from his extensive experience on the diagnosis and management of osteoporosis and osteomalacia, and there are chapters on the orthopaedic aspects of haemophilia, problems of the forefoot and paediatric osteomyelitis.

The book is well produced and the illustrations are numerous and of good quality. The reviewer read it with interest and profit.

R. BARNES

Accident Surgery and Orthopaedics for Students

J. R. Pearson, Birmingham, and R. T. Austin, Leicester. 248×184 mm. Pp. 218+xiv. 1973. London: Lloyd-Luke (Medical Books) Ltd. £2·75.

THE declared purpose of the authors of this book was to produce a single volume text dealing with orthopaedics and accident surgery in a concise, practical but informative manner for medical students. They have succeeded in their intention by producing a valuable aid and guide not only for medical students but also for junior staff working in accident and emergency departments. The layout of the book has been well considered in regard to easy reference, which is important to those for whom it is designed. Inevitably, there must be some personal criticisms about emphasis, but, bearing in mind the object of the book, these are few and the text is generally well balanced. The opportunity of condemning the use of equine anti-tetanic serum as a means of achieving specific immunity if there is a special risk might have been taken in view of the increasing availability of human tetanus immunoglobulin.

This book does not cover all the problems encountered in accident and emergency departments, but it provides a valuable and appropriate contribution to the areas of accidents and orthopaedics. It can be recommended not only to individuals but also for inclusion in departmental libraries. The price is certainly reasonable.

DAVID M. PROCTOR

The Cervical Spine

Robert Wayne Bailey, Detroit, Michigan. 260×185 mm. Pp. 263+viii. Illustrated. 1974. London: Henry Kimpton. £9·50.

THE cervical spine is a region with such a variety of interesting, varied and challenging pathological conditions that it is surprising that previously there has been no book devoted to this subject. To quote his own words, the author has intended the book as 'a complete and informative text on the cervical spine'. There are chapters on embryology, anatomy, congenital abnormalities, injuries, degenerative diseases, infections and tumours, to name just a few.

It is with reluctance that one must state that this book has not fulfilled the author's intention. There are some excellent chapters such as those on dynamic anatomy and cine-radiography, congenital deformities and infections. However, the sections dealing with injuries are incomplete in description, classification and treatment. A student would have difficulty in obtaining guidance on the treatment of a specific fracture. Cervical spine degeneration is better described in current journals; clinical anecdotes replace a more detailed study of the subject.

The illustrations are radiographs to a large extent. Many of these are of poor quality. Some are so bad that the normal anatomy cannot be seen, let alone the pathological changes.

It is regrettable that the poor sections of this book may prevent the reading of the better chapters.

E. L. TRICKEY

Reviews and notices of books

Pathology of the Cardiomyopathies

Brian McKinney, London. 224×150 mm. Pp. 594+xii. Illustrated. 1974. London: The Butterworth Group. £12·75.

It has been a pleasure to study this splendid book by Dr McKinney, who presents a comprehensive account of the clinical and anatomical pathology of the cardiomyopathies—those diseases of the heart not directly due to lesions of the coronary arteries or valves, or to systemic hypertension or congenital cardiovascular malformations. He has read extensively and brought together into one handy volume information widely scattered in the world literature to supplement his own long experience in this difficult field, dating from his early work in Africa. The reviewer found the sections on tropical and animal cardiomyopathies particularly valuable, for these have been a special interest of the author, but there are reliable accounts, with full bibliographies, of almost every condition which the pathologist (and clinician) must consider in the clinicopathological investigation of mysterious heart failure, and at the last 'court of appeal', as it were, in fatal cases.

The account is in two main parts. The first, shorter section deals with 'primary' cardiomyopathies, and the second, longer one with 'secondary' cardiomyopathies. As with most suggested classifications, the dividing line between primary and secondary types is blurred, and several of the author's primary types (e.g. Refsum's syndrome, oxalosis, Friedreich's ataxia) really belong to the secondary group by his own definitions; however, this is an unimportant detail.

The illustrations are good, and printer's errors commendably few and trivial (apart from the reference to Refsum's syndrome on p. 83). Heading 'strengths' are in places inconsistent and a little confusing, but this can be remedied easily in the next edition. The price seems high but not excessive considering that specialist book costs have more than doubled in the past 10 years.

Dr McKinney's many friends are delighted that he has been able to bring his work to fruition. Despite obstacles which would have daunted those of lesser courage, he has written a book of great value which will find a worthy place in all departments of pathology and cardiology. Congratulations.

REGINALD E. B. HUDSON

Surgery of the Lung. The Coventry Conference

Edited R. E. Smith, Warwickshire, and W. G. Williams, Coventry. 222×145 mm. Pp. 276+xiv. Illustrated. 1974. London: The Butterworth Group. £6·50.

The postgraduate conference held in Coventry in 1973 on lung surgery is a sequel to a previous conference held in that centre on oesophageal surgery. The success of the conferences is reflected in this well-produced publication.

The subjects presented range from the assessment, treatment and results of surgery for bronchogenic carcinoma to clinical lung transplantation. All the discussions are reported.

Surprising variation in the criteria of operability of carcinoma of the lung still exists. Mediastinoscopy clearly is a useful method of assessing operability, but again appears to be very 'operator'-dependent. The technique has reduced the incidence of failed thoracotomies for carcinoma of the lung.

Techniques in the surgery of the trachea are well reported by Dr Pearson of Toronto. Benign strictures of the trachea following long term ventilatory support have provided a large experience in North America, compared with that seen in the United Kingdom.

The methods of bronchoplastic repair, in particular sleeve resection of the lung, are well covered. This is particularly appropriate, since this technique was first performed and pioneered in England by Price-Thomas in 1947.

Clinical lung transplantation is not attended with the success accorded to the kidney or the heart. The technical, pathophysiological and immunological work described is impressive. The degree of failure in the experimental field is still high, although much of the work is carried out in dogs and this may be a species-dependent phenomenon. Up to the present time there have been no long term survivors—long term = greater than 1 year—following human lung transplantation, and of the short term survivors, one lived for 9 months, the majority not living for more than 2 months.

The contributors to this conference are all leaders in their respective area, and therefore the book presents an up-to-date compendium of current practice in surgery of the lung, trachea and major bronchi.

CHRISTOPHER LINCOLN

Book notices

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

Orthopedie Traumatologie 1972
S. Baux, J. Bedouelle, M. Bombart, J. Desbrosses, J. Lagrange, P. Masse, J. P. Razemon, and J. Vidal. 175×225 mm. Pp. 176, with 111 illustrations. 1974. Paris: L'Expansion scientifique français. 65F.

Chirurgie der Gegenwart. Number 5, Volumes 2 and 4
Edited Rudolf Zenker, München, Franz Deucher, Aarau, and Wilhelm Schink, Klön. 260×180 mm. Pp. 42+96. Illustrated. 1973. München: Urban & Schwarzenberg. No price given.

A Companion to Medical Studies. Volumes 1 and 2
R. Passmore and J. S. Robson. 275×218 mm. Vol. 1. Pp. 1276+xxii. Illustrated. Vol. 2. Pp. 1135+xxii. Illustrated. 1974. Oxford: Blackwell Scientific Publications. £8 each.

Environmental Health Perspective. Number 5
US Department of Health, Education and Welfare. 260×200 mm. Pp. 313+iv. Illustrated. 1973. North Carolina: US Department of Health, Education and Welfare. No price given.

Foot Disorders, Medical and Surgical Management
Nicholas J. Giannestras, Cincinnati, Ohio. Second edition. 260×184 mm. Pp. 669+xii. illustrated. 1973. London: Henry Kimpton. £16·85.

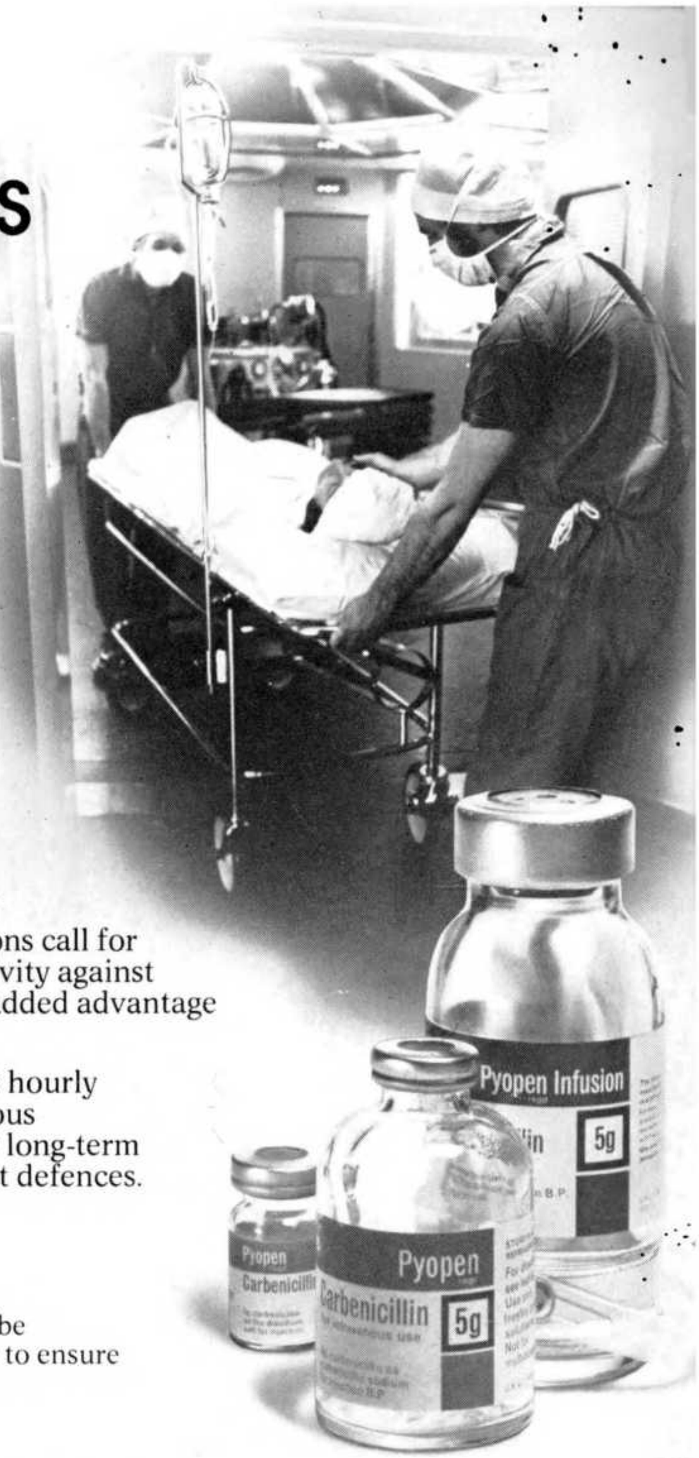
Multivariate Analysis and Psychological Theory
Edited Joseph R. Royce, Canada. 235×160 mm. Pp. 567+xvi. Illustrated. 1973. London: Academic Press Inc. £8·20.

Current Practice of Biliary Surgery
Gabriel A. Kune, Melbourne. 241×165 mm. Pp. 419+xxii. Illustrated. 1972. Edinburgh: Churchill Livingstone. £8.

The Influences of Pancreatic Tumours on the Stomach
Robert M. Zollinger and David W. Coleman, Ohio. 235×160 mm. Pp. 205+xiii, with 83 illustrations. 1974. Springfield, Ill.: Charles C. Thomas. No price given.

Isolated Organ Perfusion
Edited H. D. Ritchie, London, and J. D. Hardcastle, Newcastle. 222×140 mm. Pp. 214, illustrated. 1973. London: Crosby Lockwood Staples, Granada Publishing. £5·75.

When pseudomonas threatens...



Pyopen

The skill of the surgical team,
hours in the theatre, the most advanced
techniques in the world . . . and infection
can still throw the outcome into jeopardy.

Systemic pseudomonas or proteus infections call for Pyopen. Only Pyopen offers you good activity against these Gram-negative organisms with the added advantage of penicillin safety.

Intravenous Pyopen, at a dosage of 5g 4–6 hourly will rapidly control many of these dangerous infections. And Pyopen is also suitable for long-term therapy and for patients with lowered host defences.

Adult Dosage
5g I.V. 4–6 hourly.
In patients with renal impairment dosage may be reduced; monitoring is advisable in these cases to ensure adequate serum antibiotic levels.
Contra-indication
Penicillin hypersensitivity.
Side-effects
As with other injectable penicillins. In rare cases, skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Pyopen–by infusion or injection

Further information is available on request.
Pyopen* (carbenicillin sodium B.P.) is a British product originated by
Beecham Research Laboratories, Brentford, England *regd

H. K. Lewis & Co. Ltd.

Medical Publishers
and Booksellers

136 GOWER STREET
LONDON, WC1E 6BS

Telephone : 01-387 4282

LEWIS'S
MEDICAL LIBRARY

Annual Subscription from £4·00

Books may be exchanged as often as desired. There are reduced rates for multiple subscriptions.

Prospectus post free on request

The Choroid Plexus in Health and Disease

Edited by M. G. NETSKY, MD, *Professor of Neurosurgery, University of Virginia School of Medicine;* and S. SHUANGSHOTI, MD, *Assistant Professor of Pathology, Chulalongkorn University, Bangkok, Thailand*

363 pages 195 illustrations £20·00 net

A Synopsis of Surgical Anatomy

11th Edition

D. J. du PLESSIS, ChM(Rand), FRCS(Eng), *Head of Department of Surgery, University of the Witwatersrand, Johannesburg; Chief Surgeon, Johannesburg General Hospital*

About 900 pages 779 illustrations About £7·00 net

Biochemical Values in Clinical Medicine

5th Edition

R. D. EASTHAM, MD, MRCP, FRCPath, DCP, Dipl Path, *Consultant Pathologist to the Frenchay Group of Hospitals, Bristol*

This book provides an accurate summary of the ways in which various conditions affect many biochemical tests, in each case giving the normal values and a commentary on the interpretation of results attained. Knowledge of the significance of abnormal results of biochemical tests continues to expand and this fifth edition has been extensively revised with the inclusion of some thirty new sections, including various auto-immune antibody tests, polypeptide hormone estimations, therapeutic drug levels and notes on the value of amniocentesis in antenatal biochemical detection of inherited disease and on interlaboratory results of various tests. This quick-reference pocket book will continue to be invaluable.

238 pages £2·00 net

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

ACM endoscopes leave nothing to the imagination

st surgeons today recognise the superiority of endoscopy as a ans of confirming diagnoses of colon diseases. It can be quicker d easier than laparotomy, and is also less traumatic for patients and kes fewer demands on hospital facilities.

The premier instrument for colonic investigations is the ACM F9L oscope. Advanced features include 12X magnification and a sharp, de angle circular image three times larger than competitive trument's.

With it a surgeon can clearly view as far as the caecum, take biopsy ecimens and perform polypectomies. After surprisingly little actice, colоscopy can be most rewarding. And the ACM coloscope exceptionally easy to use – a single, one-handed joystick controls e poly-directional tip.

There's a shorter version, too, the F9S which will reach to the nsverse colon and beyond. For the experienced coloscopist there's the dual channel F9A, a major operative, as well as diagnostic instrument.

To find out more, please use the coupon. Or write or telephone.

Please tell me more about ACM endoscopes.
I would like literature only ________ ☐
Please arrange a visit
My telephone number is ________ ☐
Name ________
Address ________
____
________ B.J.S 3-75

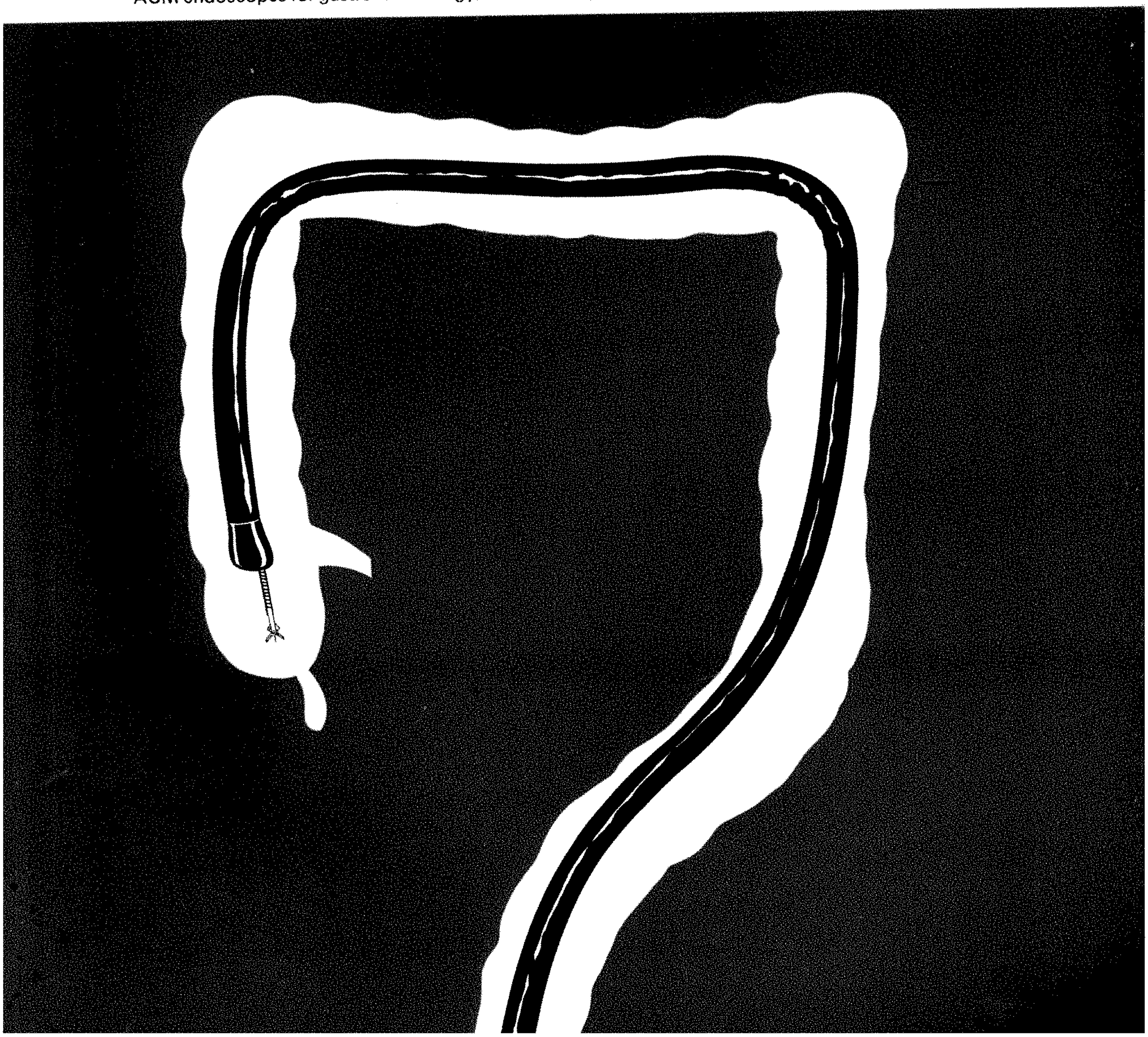
ACM Endoscopes – clearly the best

ACM

Wappler Endoscopy Limited,
Park House, 22 Park Street, Croydon, Surrey, CRO OYH
Telephone: 01-686 4241

WAPPLER Endoscopy Limited

ACM endoscopes for gastro-enterology, bronchoscopy, urology, gynaecology and teaching.



Sodium Fusidate

fucidin

Now the orthodox treatment for staphylococcal infections

- *Journal of Bone and Joint Surgery, 1972 (May).
- *British Medical Journal, leading article, Volume 1, page 126, 1970.
- *Journal of Bone and Joint Surgery, Volume 52B, No. 2, 1970.
- *Quarterly Journal of Medicine, Volume 38, No. 149, 1969.
- *British Journal of Clinical Practice, Volume 23, No. 1., 1969.
- *British Medical Journal, leading article, Volume 4, page 656, 1968.

and more than 160 other original publications

Further information available on request
LEO LABORATORIES LIMITED
L E O HAYES MIDDLESEX Tel: 01-573 6224

Trasylol

significantly reduces mortality and morbidity in acute pancreatitis

Trapnell, J. E. *et al.* (1974) *British Journal of Surgery*, **61**, 177.

Trasylol®

(aprotinin)

Bayer BAYER

® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

Vol. 62 : No. 4 : April 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society)
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
I. D. A. JOHNSTON Newcastle
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN McADAM Kampala : Uganda
A. C. McEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX

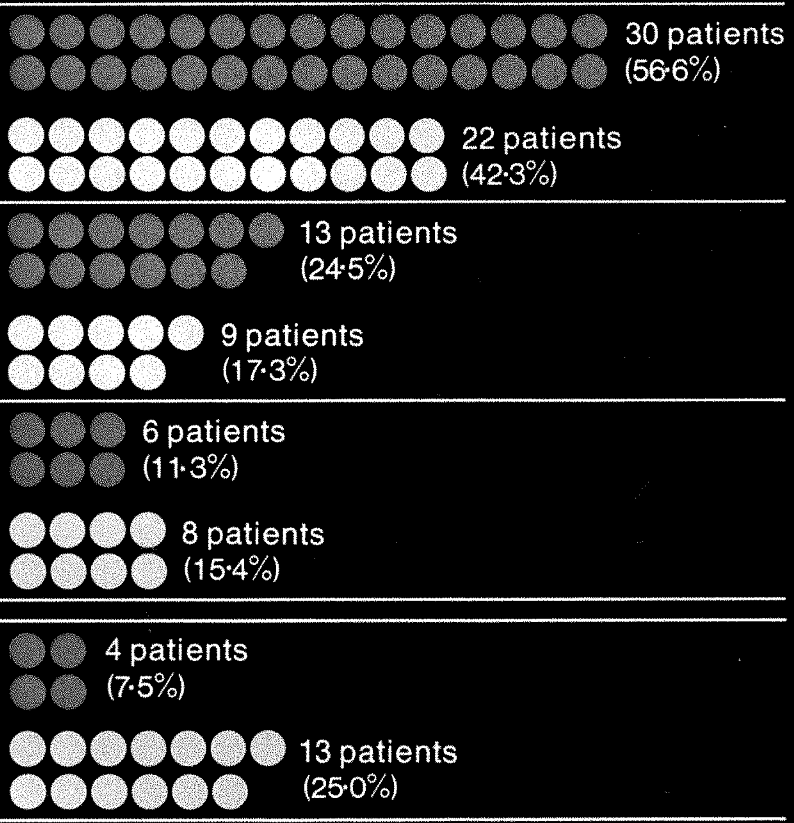
Subscription £15 per annum, post free. Single copies £1·50, post free

---

THE WILLIAMS & WILKINS CO., BALTIMORE
Second Class Postage paid at Baltimore, and at additional mailing offices.

The new evidence for Trasylol in the treatment of acute pancreatitis

Prospective double-blind trial in 105 patients over a five year period shows Trasylol to significantly reduce mortality and morbidity in acute pancreatitis.[1]



Course of illness	
Mild	30 patients (56·6%) 22 patients (42·3%)
moderate	13 patients (24·5%) 9 patients (17·3%)
severe	6 patients (11·3%) 8 patients (15·4%)
DIED	4 patients (7·5%) 13 patients (25·0%)

● Trasylol group (53)
○ placebo group (52)

'Trasylol must therefore be regarded as a drug which is beneficial in the treatment of acute pancreatitis.'[1]

[1] Trapnell, J.E. *et al.* (1974) *British Journal of Surgery*, **61**, 177

Trasylol®

(aprotinin)

Bayer

® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

The British Journal of Surgery

Vol. 62 : No. 4 : April 1975

Original papers

		Page
The importance of environmental conditions, especially temperature, in the operating room and intensive care ward	Lord Brock	253
Some observations on peripheral venous pressure using a non-invasive technique: a preliminary report	H. Gaylis	259
Report of a family with inherited medullary carcinoma of the thyroid and phaeochromocytoma	J. M. Beaugie, P. E. Belchetz, C. L. Brown, R. J. Frankel and Margaret H. Lloyd	264
Neoplastic change in duplications of the alimentary tract	M. M. Orr and A. J. Edwards	269
A controlled trial of parenteral prophylactic gentamicin therapy in biliary surgery	M. R. B. Keighley, R. M. Baddeley, D. W. Burdon, J. A. C. Edwards, A. H. Quoraishi, G. D. Oates, G. T. Watts and J. Alexander-Williams	275
Operative biopsy of the pancreas	Phyllis George, Colin Brown and James Gilchrist	280
Carcinoma of the large bowel in the Sudan	S. H. ElMasri and P. B. Boulos	284
A controlled clinical trial of three different methods of perineal wound management following excision of the rectum	T. T. Irvin and J. C. Goligher	287
Povidone-iodine for the control of surgical wound infection: a controlled clinical trial against topical cephaloridine	A. V. Pollock and Mary Evans	292
Bacteria in flower vase water: incidence and significance in general ward practice	C. A. Bartzokas, Marguerite P. Holley and Christine A. Sharp	295
Analgesic abuse in urological practice	R. W. Parker and Richard E. Shaw	298
The Fowler–Weir approach to appendicectomy	A. R. Askew	303
Subphrenic abscess in children	M. MacKenzie, J. Fordyce and D. G. Young	305
The cause and treatment of postvagotomy diarrhoea	John R. Condon, V. Robinson, M. I. Suleman, V. S. Fan and M. D. McKeown	309
Possible parathyroid origin of gastrin in a patient with multiple endocrine adenopathy type I	J. Cassar, J. M. Polak and W. M. Cooke	313
The cholecystokinin test: an assessment	D. R. K. Reid, I. M. Rogers and J. F. Calder	317
Intra-abdominal symptoms arising from spinal osteophytes	S. S. Rawat, G. K. Jain and H. K. D. Gupta	320
Tuberculous peripheral lymphadenitis in the Igbos of Nigeria	Wilson I. B. Onuigbo	323
Gynaecomastia	D. B. Hamer	326
Cavernous haemangioma of the frontal bone: case report	S. D. Gupta, I. N. Tiwari and N. K. Pasupathy	330

Reviews and notices of books 333

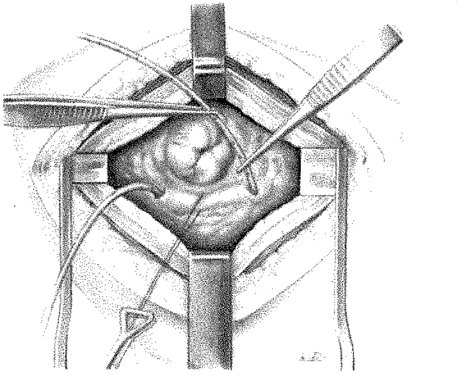
© John Wright & Sons Ltd and the respective contributors named above. 1975.
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any other form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.

Nouveau traité de technique chirurgicale
New treatise on surgical technique
Volume XV: Urology

by R. Couvelaire and J. Cukier
published under the direction of
J. Patel and L. Leger

This superbly illustrated volume is consecrated to the surgery of the urinary apparatus (kidneys, ureters, vesica, urethra) and the male genital apparatus (testicles, epididymis, spermatic ducts, prostate). The authors carefully signal foreseeable difficulties and, whenever appropriate, analyse the indications and counter-indications for a given mode of action. An authoritative guide to the principles and particularities of each operation.

Text in French. ISBN 2-225-39358-3. 848 pp., 993 fig., 335 francs (in January 1975).



- *For additional information about this or other volumes, please contact MASSON, 120 bd. St-Germain, F 75280 Paris cedex 06.*
- *In the U.S.A., orders may be placed directly with S.M.P.F., Inc., 110 West 57th Street, Suite 317, New York, N.Y. 10019.*

MASSON

BRITISH JOURNAL OF SURGERY

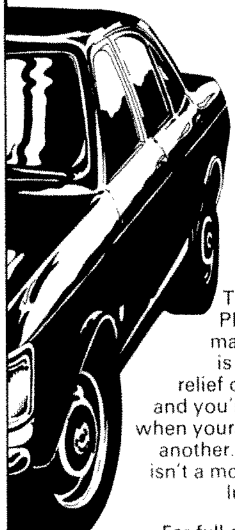
Binding Cases

Binding cases for Volume 61 may be obtained from the Publishers at £2·00 post free. They are supplied in dark red cloth with imitation gold lettering on the spine.

If desired, the publishers will undertake the binding at an inclusive charge of £7·50, post free.

JOHN WRIGHT
42–44 TRIANGLE WEST
BRISTOL BS8 1EX

NEW CAR?



NO CAPITAL OUTLAY

The Clearway Executive Leasing Plan offers you the choice of any make or model, what's more there is no capital outlay and 100% tax relief on your annual leasing charges, and you're never without a car, because when yours is being serviced we lend you another. For the professional man there isn't a more economical way of ensuring luxurious, trouble free motoring.

For full details contact:
Clearway Leasing, 11 Belmont, Lansdown Road,
Bath BA1 5DZ (Tel: 60463)
An Oliver Rix Company

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 60. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISEMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are two or more authors (apart from the main author), these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title

of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature* (*Lond.*) **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea 4, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th ed. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology.* London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BEAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

Congress Proceedings

CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding. or that following.,

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)

Fight cancer with a will

When testators ask your advice, please remind them of the urgent work of the Imperial Cancer Research Fund. In the Fund's up-to-date laboratories trained minds are using every weapon of modern science to fight all forms of cancer, including leukaemia.

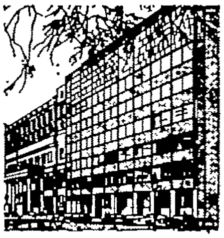
Now one of the world's great research centres, the I.C.R.F. relies entirely on public support. The cancer problem *must* be solved. Please help now.

Patron:
H.M. THE QUEEN
President:
The Honourable Angus Ogilvy

Form of Bequest

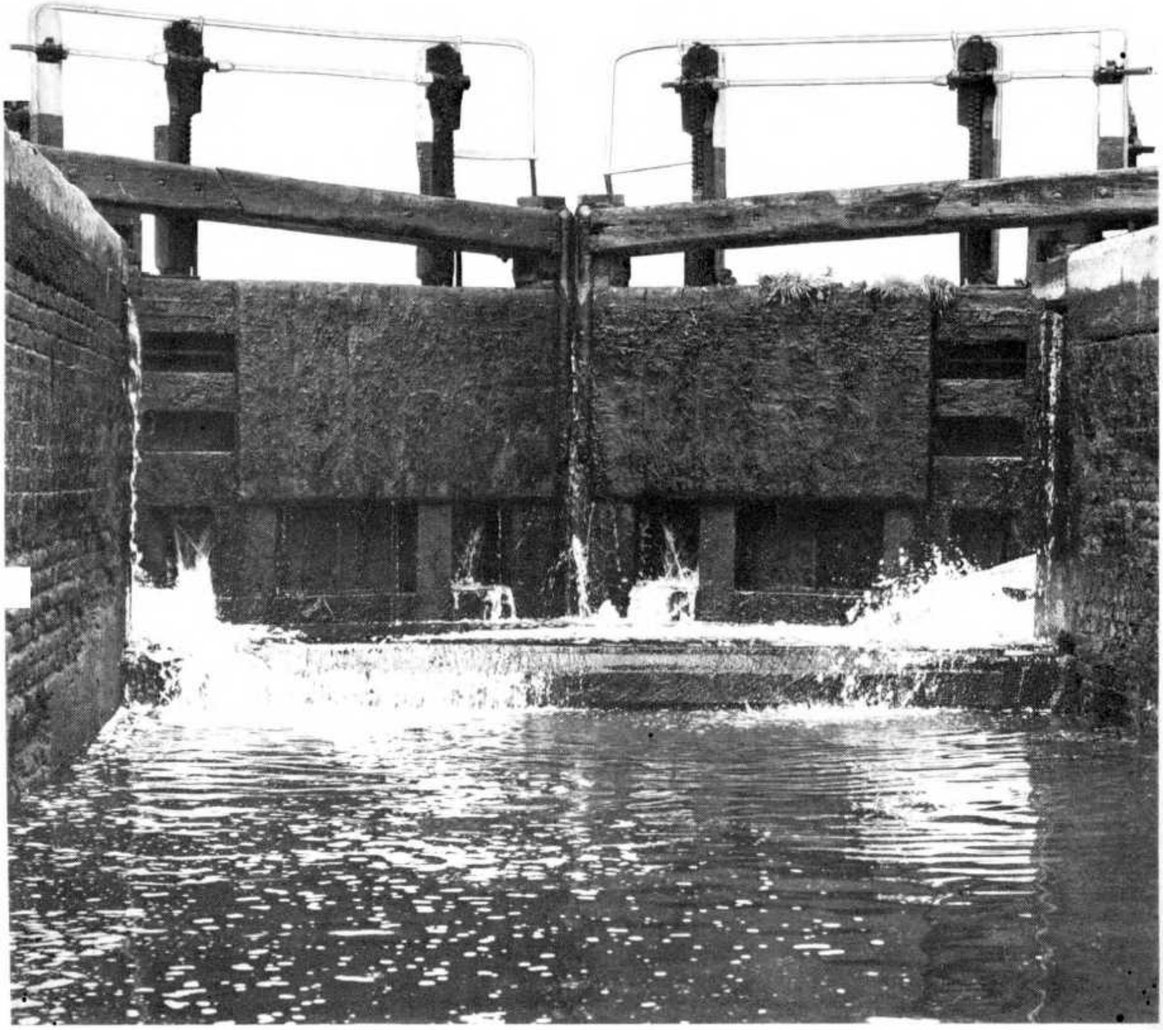
I hereby bequeath the sum of.................pounds free of duty to the Imperial Cancer Research Fund, Lincoln's Inn Fields, London, WC2A 3PX for the purpose of scientific research, and I direct that the receipt of the Honorary Treasurer or Secretary shall be a good discharge for such legacy.

Please write for further information to: The Secretary, I.C.R.F. (Dept 164), PO Box 123, Lincoln's Inn Fields, London WC2A 3PX

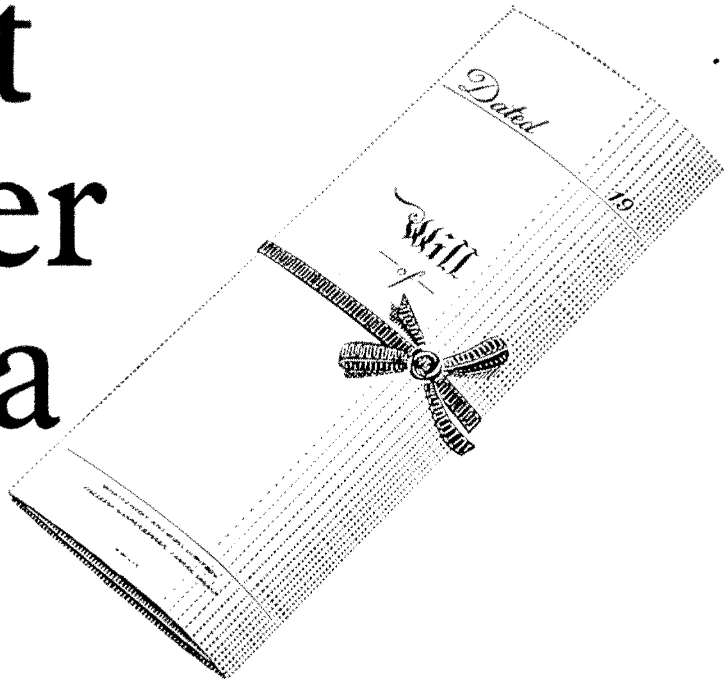

Lincoln's Inn Fields Laboratories

IMPERIAL CANCER RESEARCH FUND

A new concept in the control of occlusive vascular disease



Fight cancer with a will



When testators ask your advice, please remind them of the urgent work of the Imperial Cancer Research Fund. In the Fund's up-to-date laboratories trained minds are using every weapon of modern science to fight all forms of cancer, including leukaemia.

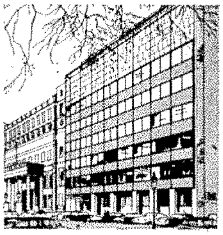
Now one of the world's great research centres, the I.C.R.F. relies entirely on public support. The cancer problem *must* be solved. Please help now.

Patron:
H.M. THE QUEEN
President:
The Honourable Angus Ogilvy

Form of Bequest

I hereby bequeath the sum of..................pounds free of duty to the Imperial Cancer Research Fund, Lincoln's Inn Fields, London, WC2A 3PX for the purpose of scientific research, and I direct that the receipt of the Honorary Treasurer or Secretary shall be a good discharge for such legacy.

Please write for further information to: The Secretary, I.C.R.F. (Dept 164),
PO Box 123, Lincoln's Inn Fields, London WC2A 3PX

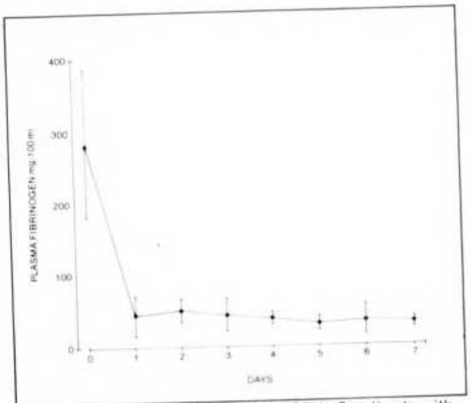

Lincoln's Inn Fields Laboratories

IMPERIAL CANCER RESEARCH FUND

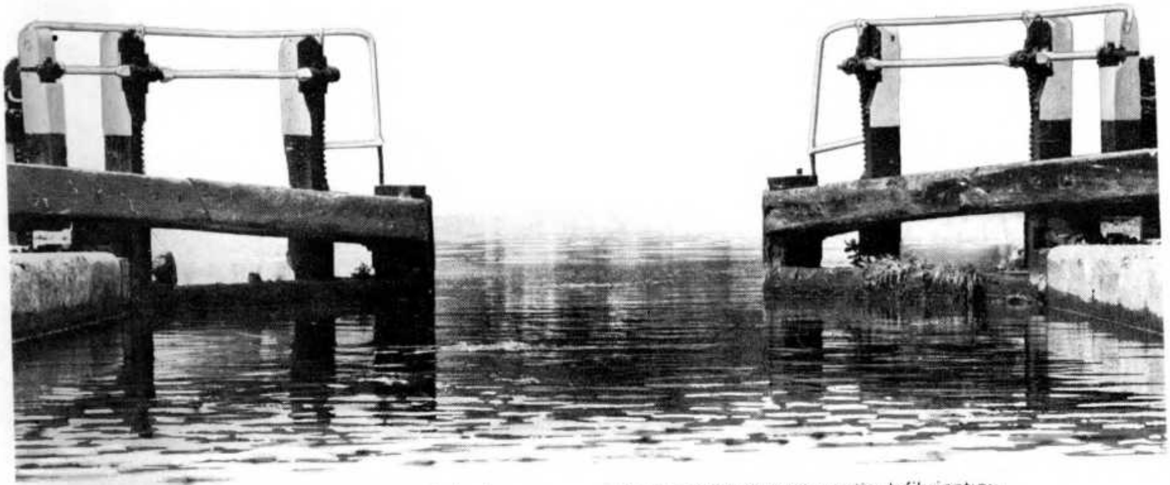
A unique drug is now available to the specialist for routine anticoagulant therapy, and to the researcher as an aid to the elucidation of thromboembolic disorders. Its name is Arvin.

Arvin reduces plasma fibrinogen to a level that maintains marked hypocoagulability without serious spontaneous bleeding complications. This desirable effect is achieved through the specificity of Arvin for fibrinogen—other clotting factors are unaffected.

This state of 'pure' defibrination has an important clinical place when prophylactic measures need to be taken in occlusive vascular disease. e.g. to prevent the formation and extension of thrombi and the dissemination of emboli.



Mean plasma fibrinogen level ± SD in 9 patients with venous thromboses. Arvin 2 units/kg body weight intravenously every 12 hours. From Pitney WR, (1971). Thromb Diath Haemorrh, *45*, 43.



Consistent features of Arvin therapy include an absence of thromboembolic events during treatment, absence of fibrinogen rebound and low incidence of rethrombosis after treatment has ceased. On withdrawal, plasma fibrinogen returns to haemostatic levels within 12 hours and to normal after 10-20 days. Thus, the changeover to oral anticoagulants is smooth and complication-free.

A consistent dose-effect relationship which ensures simple and precise control methods has been established for Arvin. On this basis, we can recommend this drug for a range of indications where controlled therapeutic defibrination is desirable.

For instance, deep vein thromboses, central retinal and branch vein thrombosis, priapism, pulmonary hypertension of embolic origin, embolism after prosthetic cardiac surgery and rethrombosis after thrombolytic therapy have been shown in clinical trials to respond well to Arvin.

To find out more about the unique Arvin concept specialists are invited to write to us for detailed clinical literature and prescribing information.

Arvin
ancrod
controlled therapeutic defibrination

J4591

Berk Pharmaceuticals. Shalford, Surrey.

Arvin is a registered trademark

Synopsis of Anaesthesia

7th Edition

J. ALFRED LEE, FFARCS, DAHon FFARCSI, *Honorary Consulting Anaesthetist to the Southend-on-Sea Hospital;* and R. S. ATKINSON, MA, MBBChir, FFARCS, *Consultant Anaesthetist, Department of Anaesthetics, Southend-on-Sea Hospital.*

'It is a true compendium of knowledge which will be read avidly by every examinee throughout the world. The authors deserve the highest praise for producing such a worthy volume.' *World Medicine*

1000 pages 31 illustrations £5·00 net.

Synopsis of Surgical Anatomy

11th Edition

D. J. Du PLESSIS, ChM(Rand), FRCS(Eng), *Head of Department of Surgery, University of the Witwatersrand, Johannesburg; Chief Surgeon, Johannesburg General Hospital.*

About 900 pages 779 illustrations £7·00 net.

The Choroid Plexus in Health and Disease

Edited by M. G. NETSKY, MD, *Professor of Neurosurgery, University of Virginia School of Medicine;* and S. SHUANGSHOTI, MD, *Assistant Professor of Pathology, Chulalongkorn University, Bangkok, Thailand.*

363 pages 195 illustrations £20·00 net.

Essentials of Urology

D. E. STURDY, MS, FRCS, *Surgeon, Royal Gwent Hospital, Newport, Mon.*

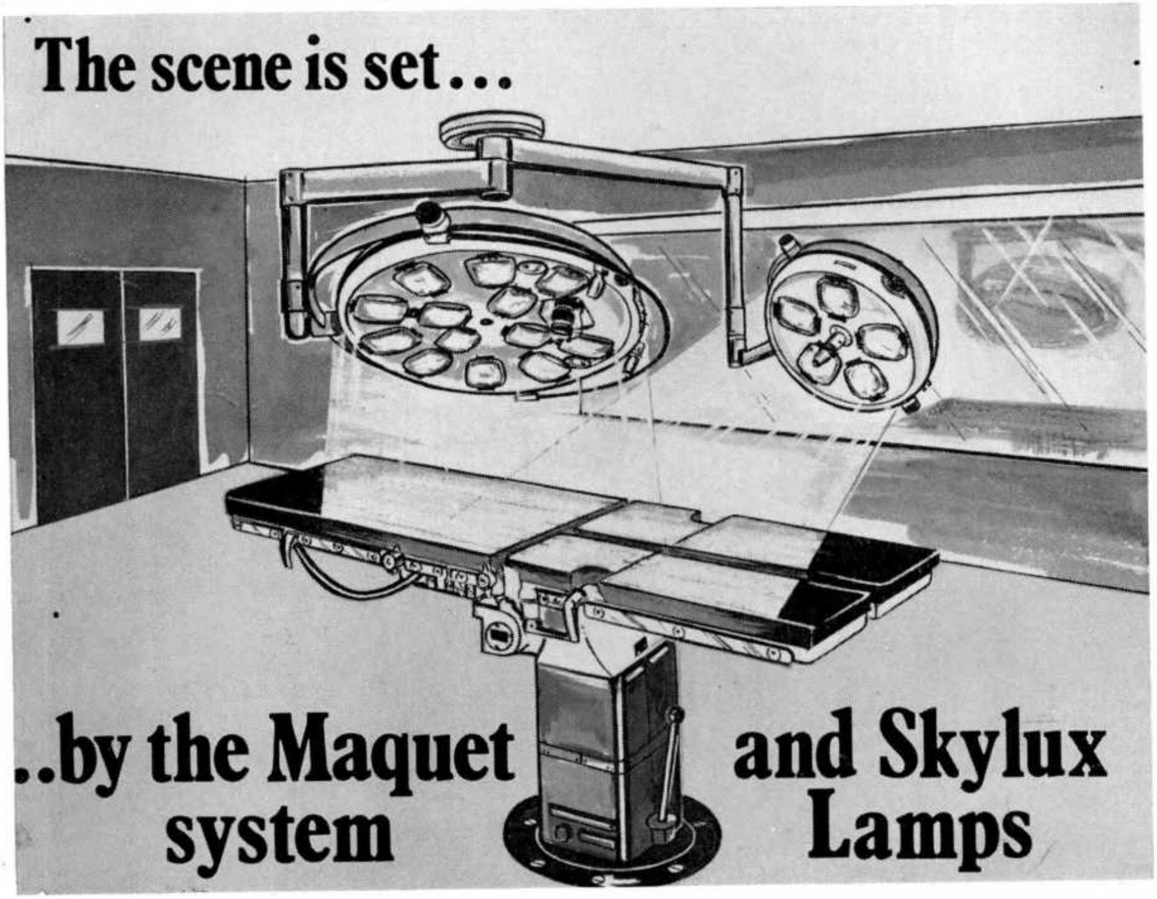
'The book will no doubt be read by many young people, because it is easy to read and it fills a gap in the urological shelves of hospital libraries.' *British Medical Journal*

'This is a well-written, well-illustrated book, more than adequate for the undergraduate, valuable to the postgraduate.' *General Practice*

'This book fills a need, particularly for the medical student and the candidate for a general surgical postgraduate degree. . . . The line drawings are clear, and the radiographic reproductions are excellent and clearly illustrate the text.' *South African Medical Journal*

306 pages 215 illustrations £5·00 net.

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX



Maquet fixed column operating table system

- Fixed column–power operated
- Extreme stability
- Free access for x-ray equipment
- Wide variety of table tops
- Tops easily interchangeable–increased theatre efficiency
- Unique 'Tele' control
- Easy clean finish

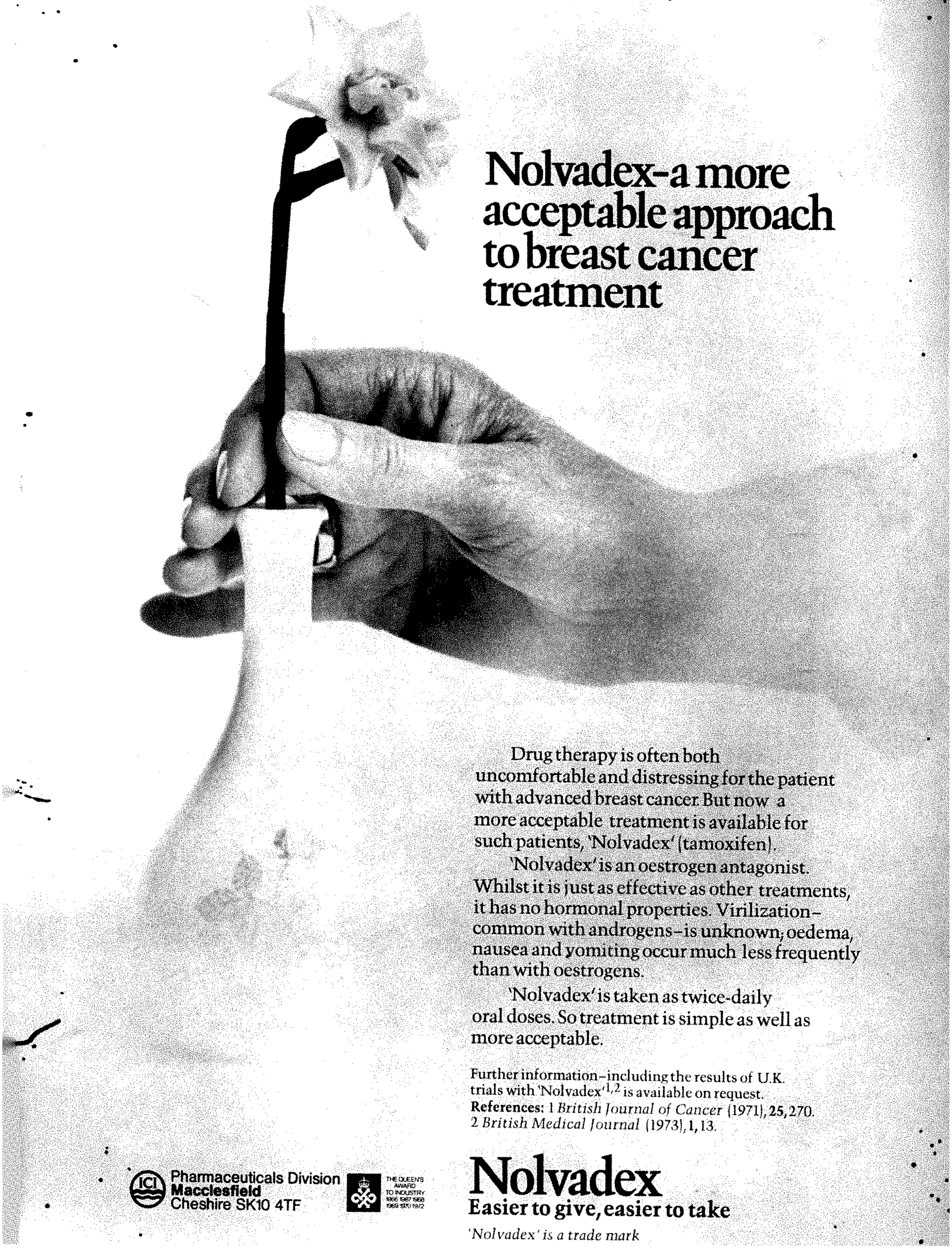
Skylux Lamps – for all Theatre applications

- High level of light intensity
- Maximum freedom from shadow and glare
- Ideal variation of illumination
- Heat free
- A real white light
- Easy mobility

Catalogues available on request

Downs Surgical Ltd

CHURCH PATH, MITCHAM, SURREY 01-648 6291



Nolvadex-a more acceptable approach to breast cancer treatment

Drug therapy is often both uncomfortable and distressing for the patient with advanced breast cancer. But now a more acceptable treatment is available for such patients, 'Nolvadex' (tamoxifen).

'Nolvadex' is an oestrogen antagonist. Whilst it is just as effective as other treatments, it has no hormonal properties. Virilization–common with androgens–is unknown; oedema, nausea and vomiting occur much less frequently than with oestrogens.

'Nolvadex' is taken as twice-daily oral doses. So treatment is simple as well as more acceptable.

Further information–including the results of U.K. trials with 'Nolvadex'[1,2] is available on request.
References: 1 *British Journal of Cancer* (1971), **25**, 270.
2 *British Medical Journal* (1973), **1**, 13.

ICI Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

THE QUEEN'S AWARD TO INDUSTRY 1966 1967 1968 1969 1970 1972

Nolvadex

Easier to give, easier to take

'Nolvadex' is a trade mark

The British Journal of Surgery

Vol. 62 : No. 4 : April 1975

Br. J. Surg. Vol. 62 (1975) 253–258

The importance of environmental conditions, especially temperature, in the operating room and intensive care ward

LORD BROCK*

SUMMARY

Although most patients are essentially well enough to be able to resist or to adapt to unfavourable ambient conditions, this may not be so with an ill patient or one who is having or has had a serious operation. The climatic conditions necessary in the operating room to give an optimal environment are discussed. These are second in importance only to control of infectivity. Air-conditioning in operating suites should be obligatory; there is even official acceptance of this. Earlier recommendations that the operating room should be heated to up to 80 °F (27·9 °C) are obsolete. The temperature most favoured by surgeons is 18·5–21 °C; some prefer a range of 21–22 °C. The critical ambient temperature desirable is 21 °C. For infants and children this may be increased up to 24 °C. It is difficult or impossible to achieve climatic conditions in the operating room that are acceptable to all. The needs of the patient are of special importance and are largely neglected; he alone is unable to speak for himself. The disposition of air inlets in the operating room is fully discussed.

Climatic conditions in the intensive care unit are of great importance and are discussed. The need for full air-conditioning is absolute although this is often ignored. The delivery of conditioned air within the intensive care unit is also fully presented, especially the need to avoid direct chilling of the patient. The advantages of horizontal laminar air flow are presented.

THE importance of a study of central and peripheral temperatures in the recognition of hypovolaemia after open heart surgery was presented in the report of a case (Spitzer and Brock, 1968). A later article (Ross et al., 1969) on observations of central and peripheral body temperatures in the understanding and management of shock dealt with the valuable information that can be obtained essentially in regard to hypovolaemia as a major cause of shock. This work was based on the report of Ibsen (1967) on this subject.

Prolonged experience with the study of central and peripheral temperatures and of the gradient between them has served to reinforce the statement (Ross et al., 1969): 'we now feel unable to manage the care of a patient potentially or acutely ill without having information that temperature studies give'. It still remains true that 'few people are aware of such studies and we have even been told that all the information we are presenting is available by a simple touch of the hand on the nose or the feet of the patient.' Far from this information being of little value the present author remains convinced that much can be learned from it.

Most patients are essentially well enough to be able to resist or to adapt satisfactorily to unfavourable conditions so that these often do not matter greatly. It is different with an ill patient or with one who is having or has had a serious operation.

Let us first consider the significance of the climatic conditions in the operating room to which the patient and members of the operating team are exposed. Much has been written about this in recent years but the extent to which practical measures have been taken to achieve an optimal or even improved environment has varied considerably. It is important that the fullest consideration should be given to all the problems involved in view of the very large sums of money that are being spent on hospital construction and that will affect the comfort and recovery of patients and also the life and work of doctors, nurses and of many others for decades or even generations to come.

Amongst the many publications on these matters attention is drawn to the Report of a Committee of the Royal College of Surgeons (1964) on 'design of operating theatre suites'. The most important factors relevant to the design of operating suites are those concerned with the avoidance or minimization of infection; clearly these are paramount. The transition from the old operating theatre through antiseptic to aseptic conditions was a brilliant and revolutionary achievement. Next in importance is the provision of

---

* Department of Surgical Sciences, Royal College of Surgeons, London.

suitable climatic conditions for all those within the operating suite, including the patient.

It used to be taught that it was in the patient's interest for the temperature in the operating room to be between 70 and 80 °F. One well known and popular textbook of surgery states 'The theatre . . . must be equipped with a heating system capable of maintaining a temperature of up to 80 °F.' That is 27 °C!

Without air-conditioning the operating room can be uncomfortable and conditions may become intolerable. Operating room temperatures during the summer in the city of New York have reached the high 90's with associated high humidity and consequent hyperpyrexia developing (Clark and Ravenstine, 1954). Such conditions are almost obsolete in the USA now that air-conditioning is used. In Great Britain the need for air-conditioning in operating suites is by no means generally accepted (Ministry of Health, 1967). Happily, reason is prevailing and there is wide, even official, acceptance of the absolute need for full air-conditioning in most operating rooms (Medical Research Council and Department of Health, 1972). It is necessary to emphasize that air-conditioning must include control of temperature and humidity and does not mean just forced ventilation.

Two other comments are appropriate at this point. The first is relative to the post-anaesthetic recovery area (that surely must be treated exactly as the operating room) and to the intensive care unit.

The introduction of the intensive care unit is one of the most important and profound changes that has been seen in the clinical lifetime of most of us. Much of the organization of the intensive care unit is concerned with the measurement of parameters that give exact information about vital phenomena instead of relying on the observations and judgements of 'good nursing'. The improvements in care that result are immense, as we understand more exactly and more deeply what is going wrong with the patient and what therapeutic adjustments are needed. However, the general neglect of deliberate consideration of the environmental conditions of the patient in the intensive care unit is surprising. For example, a recent authoritative article on 'surgical intensive care' (Walker, 1973) discusses thoroughly the various parameters that must be measured but makes no mention at all of the environmental conditions that may be important causes of undue extra stress.

In a recently published special brochure devoted to intensive care *Health and Social Service Journal*, 1974) seventeen intensive care units are described and in only two is air-conditioning mentioned as being included in the primary design; in one other it was excluded on grounds of economy and later had to be added. In none of the other fourteen is it even mentioned. It is refreshing to read in an article on the organization and design of intensive care units (Verner, 1974) 'Air-conditioning is essential in intensive care units.'

In the present author's opinion the value of the various parameters can be greatly increased by ensuring that the patient is exposed to a standard controlled environment that shields him from unfavourable ambient influences. The improvements in physiological observation and care that are so important among the aims of the intensive care unit should surely be extended to physical environment. It should be axiomatic that in planning the intensive care unit in every new hospital building provision should be made for full air-conditioning. When such a department is to be set up in an existing hospital it must necessarily be fashioned around or within existing accommodation and therefore shares the climatic disadvantages that the original wards or rooms may possess—disadvantages that may not be important in the original use of the quarters but may become extremely so in their new use.

Experience reveals examples of this, especially in regard to the weather aspect. The main outlook may be south or south-west and this can lead to intolerable conditions at certain times of the day and during some seasons of the year. Conversely, an eastern or northern aspect can produce adverse conditions at the other extreme, particularly if the wind is in an unfavourable direction. An intensive care area often has a mixture of aspects of varying types but which have the one common factor that at certain times, either of the day or of the night, they each produce or contribute to an unfavourable environment for the patient. Much can be done to mitigate this in simple ways, such as by double glazing or efficient shading; proper care should always be directed to what are often obvious and simple measures to be taken but which are just not considered or are ignored. However, the basic essential requirement is full air-conditioning.

The second comment that is inseparable from the issue arises directly from this, namely the type and design of air-conditioning to be used. The usual attitude to air-conditioning is that it is an entity like the provision of gas, water and electricity and can be requested and installed as such. This seems to be the conception of most surgeons, doctors or administrators when faced with the problem of the design of a new building or the conversion of an old one. The need to discuss with the engineers the type of air-conditioning to be installed so as to secure the best conditions is far too little appreciated. Inevitably the engineer, in most instances, is likewise unlikely to be aware of just what is required. He will have full knowledge of the basic facts of ventilation, of control of temperature, humidity and filtration etc., that he can put at the disposal of his clients but he must or should be carefully informed of exactly what is required. The installation of the plant, the trunking and the outlets will be complex and expensive and will require conformity to or alteration of building design to accommodate them. The installation will inevitably be there for many years whether it is the right arrangement or not. Close cooperation between the doctors and the engineers is essential to ensure that it is known exactly what is needed.

As the author is not an engineer the following suggestions may be incorrect, incomplete or impractical but it is hoped they will serve as a basis for discussion. The suggestions now made are not meant to be complete or final or even fully reasoned. My team is embarking on a series of observations to try to introduce method to certain recommendations or suggestions. The securing of relevant information is time-consuming and is not easy. It is hoped to report in later articles on progress on various aspects of the problems that exist as information is gained.

The basic design and function of the central plant and equipment must be the responsibility of the heating and ventilating engineers. The author is chiefly concerned with the mode of delivery of the conditioned air to the operating suite or to the intensive care unit and hence to the patient.

Let us take the operating room first; apart from the anaesthetic room the requirements of the other rooms follow almost inevitably with the essential provision that the area of highest air pressure will be the operating room and the aseptic area in general, and the arrangement of doors, windows and other features will be such as to encourage the desired scheme of air circulation or air flow. While recognizing the prime need for attaining the highest standards of asepsis, of really clean air and the avoidance of contamination from any source, space does not permit a full consideration of these; in any case much has already been written about the control of infectivity. For example, environmental surveys of the operating suites at various RAF hospitals have been well reported by the Royal Air Force Institute of Health and Medical Training (1972a, b) at Halton under the overall direction of Group Captain I. A. McIntosh; a very high standard of infectivity control is achieved with consequent lessening of the incidence of postoperative infection. The present remarks will be confined essentially to the climatic factors involved.

Mention has already been made of the modern readjustment of views on the temperature ranges desirable in the operating room and that the earlier recommendation of up to 80 °F (27 °C) is unacceptable. It should be realized, however, that it is not possible to provide the temperature conditions to suit the needs of all those working in the operating room. The surgeon, the anaesthetist, the scrub nurse, the other nursing assistants and the ancillary workers may all require different conditions. This has been well shown by the work of Wyon et al. (1968) on thermal comfort during surgical operations.

The individual who is in danger of being overlooked is the *patient* and he, of course, is the one being who is unaware of and unable to take protective action if the climate to which he is exposed is uncomfortable, undesirable or even dangerous.

It is important to recognize this difficulty or impossibility of achieving climatic conditions in the operating room that are acceptable to all. Wyon et al. (1968) found that most surgeons preferred temperatures around 66·5 °F (19 °C) at 50 per cent relative humidity and 25 ft/minute air movement, allowing for the average amount of thermal radiation from the operating room lamp. At this temperature nearly half the anaesthetists would feel too cold; they mostly preferred temperatures around 71 °F (21·5 °C). The anaesthetist is for much of the time less active than the surgeon who bears the continuing burden of the anxiety and responsibility of the operation as well as having to work in a warmer area of the room. By contrast the anaesthetist may be sitting in such a position that he is directly exposed to the air inlets that may be immediately over his head. One simple answer to these differing personal requirements among the operating room team is that they should dress accordingly; the anaesthetist, for example, may need warmer clothing. This need for adaptation of the climatic requirements of each individual becomes most important when we consider the patient himself. It is unlikely that full control of the patient's requirements of heat loss or heat gain can be achieved by adjustment of the thermal environment of the operating room, and if we are to aim to provide what is best for the patient this can only be achieved by direct methods applied to him. It is not desirable to consider this important matter more fully in this paper; it must suffice to draw attention to it now and to deal with it more fully in another article.

In addition to the varying factors that require differing conditions for the members of the operating room team we also have to face the individual preferences of the surgeon. Surgeons differ widely in what they require; many find that a comfortable working temperature is 18·5–21 °C, and it will be remembered that Wyon et al. (1968) found that most surgeons were comfortable at temperatures around 66·5 °F (19 °C) in their survey of 30 operating suites and 85 operating rooms. Some surgeons do not like a low temperature and prefer a range of 21–22 °C. It should be remembered that unless the efficiency of the surgeon is impaired by environmental conditions which are uncomfortable for him it is the effect of the temperature and humidity of the operating room on the patient that is really important. The patient may be overheated, even as far as being exposed to hyperpyrexia, or he may be chilled. Paediatric surgeons are well aware of this and it is their practice to have the theatre warmer (22–24 °C) for infants or children, especially when the operation being done or the condition being treated (e.g. burns) involves exposure and produces excessive heat loss.

Here it is necessary to consider what should be the critical ambient temperature. This has been considered and assessed by Morris and Wilkey (1970) and Morris (1971) as being 21 °C, and they recommend that to prevent intra-operative hypothermia the operating room temperature should be between 21 and 24 °C. If we accept 21 °C as the critical ambient temperature desirable for an adult this would have to be modified upwards for infants and children. Where an ambient temperature of as high as 24 °C could be accepted for the safer conduct of a high risk procedure on an ill child it would ordinarily be unacceptably warm and uncomfortable for an operating room team, even though temperatures as high or even higher than this are often inflicted on the occupants in many operating rooms. Observations will be given in a later article that do not give support to the practice of increasing the ambient temperature to prevent heat loss. In fact the principle of the exercise has been fully presented by Charles Lamb in his 'dissertation on roast pork'.

There should be wide general appreciation and awareness of the need for optimal climatic conditions in the operating room and it is suggested that it should be the proper duty and responsibility of the surgeon to make it a rule to acquaint himself with the exact conditions pertaining when he begins an operating session instead of paying little or no attention to them except to complain later that the room is too hot or too cold or too humid. For most routine operations and for short operations the climatic conditions that the patient undergoes do not matter greatly. Nature is prodigal in her endowments and patients can endure much without any great harm being done. However, if a long, complex and dangerous procedure is being undertaken, especially on an ill or a poor risk patient, then it should be incumbent upon the surgeon to acquaint himself clearly and fully with the environmental conditions in the operating room, just as he should know the relevant features of the patient's clinical state such as pulse rate, blood pressure etc., and just as the captain of a ship must know the weather conditions, the state of the tides and the draught of water.

Apart from the thermal and humidity levels it is necessary to consider the mode and site of the delivery of conditioned air into the operating room.

The use of laminar air flow, whether vertical or horizontal, is at present predominantly used for control of infectivity and it would not be useful to discuss it more fully now. At the same time it must have considerable climatic significance apart from the control of infectivity and so discussion will be necessary later.

The usual arrangement of air inlets is either by separate circular or square diffusers in the ceiling or by lateral inlets sited high up on one or more walls. The air escapes either via natural outlets such as doors, etc. or by planned outlet grilles or by pressure-relief flap valves.

It is important that the delivery of air from the inlets should not be too violent or too concentrated, and that the inlets should be sufficient in number and size to ensure a gentle inflow. Their siting must also be considered carefully and should certainly not be left for the decision of the engineer on his own. Care should be taken that they are sited in the most 'neutral' part of the room and not directly over the heads of, for example, the anaesthetists. It is tempting to the engineer if an observation dome is present to avail himself of its circular form to carry the trunking and to position the inlets around the base of the dome. This will mean that all the team who are located under the periphery of the dome are exposed to a direct down draught. In general such ceiling inlets should be more peripherally sited. Careful thought must also be given to the size and siting of air inlets on the side walls; they should be large enough and so placed that a stream of turbulent air is avoided. It is now possible to be supplied with air diffusers that do not blow down directly upon those underneath, but can direct the air inflow horizontally or in a lateral direction (*Fig.* 1). This is a simple but important consideration.

Enough has been said already to make it mandatory to provide fully conditioned air for the intensive care unit. The mode of its provision demands as much thought as in the operating room. First of all it is necessary to emphasize that the intensive care unit may need much more planned protection from harmful or unfavourable external environmental influences than does the operating room. The main weather aspect should be deliberately considered and it should not be overlooked whether it is, for example, south or north. Also any differences within the unit of the various weather aspects must be considered and protection be provided, where needed, either by appropriate shading or by double glazing. This alone can produce great benefits.

If the unit contains separate or individual rooms these will need special consideration. A common form of air inlet provided is a circular or square diffuser in the ceiling sited immediately over the patient's bed (*Fig.* 1). It is scarcely necessary to do more than draw attention to such a gross error. Similarly, in a larger ward housing several patients the siting of ceiling diffusers can be equally objectionable, not only for the patients but also for the nurses. It has already been pointed out that air diffusers can now be supplied that deliver a stream horizontal to the ceiling and *not* directly downwards. The views and experiences of the nurses are often not consulted in assessing the good or bad points of the construction of such a ward, but if asked they may be immediately forthcoming about the nuisance and drawbacks of ill-placed ceiling inlet diffusers. It will be discovered that they often find it necessary to move the patient's bed so that he may not be exposed directly to a downward air stream. The nurse may complain bitterly of this and can find it especially unwelcome if she is sitting or standing beside the bed under a downward air stream.

For reasons such as these it is necessary that the temperature controls should be conveniently adjustable in the ward and in the individual rooms. One objection often raised is that this is undesirable as nurses and others are liable to tinker with and disturb the setting. Nevertheless if the controls are inaccessible an engineer has to be summoned to alter them and this may entail much delay, especially at night.

Lateral grilles in the side walls may be unwelcome unless carefully sited. A form of laterally placed inlet that is often more satisfactory is a long slit across the whole length of one wall. If used in a single room and placed high on the wall above the patient's head it can direct the air stream in an arching fashion that passes completely over the patient and spares him from any direct discomfort while at the same time the room is efficiently ventilated.

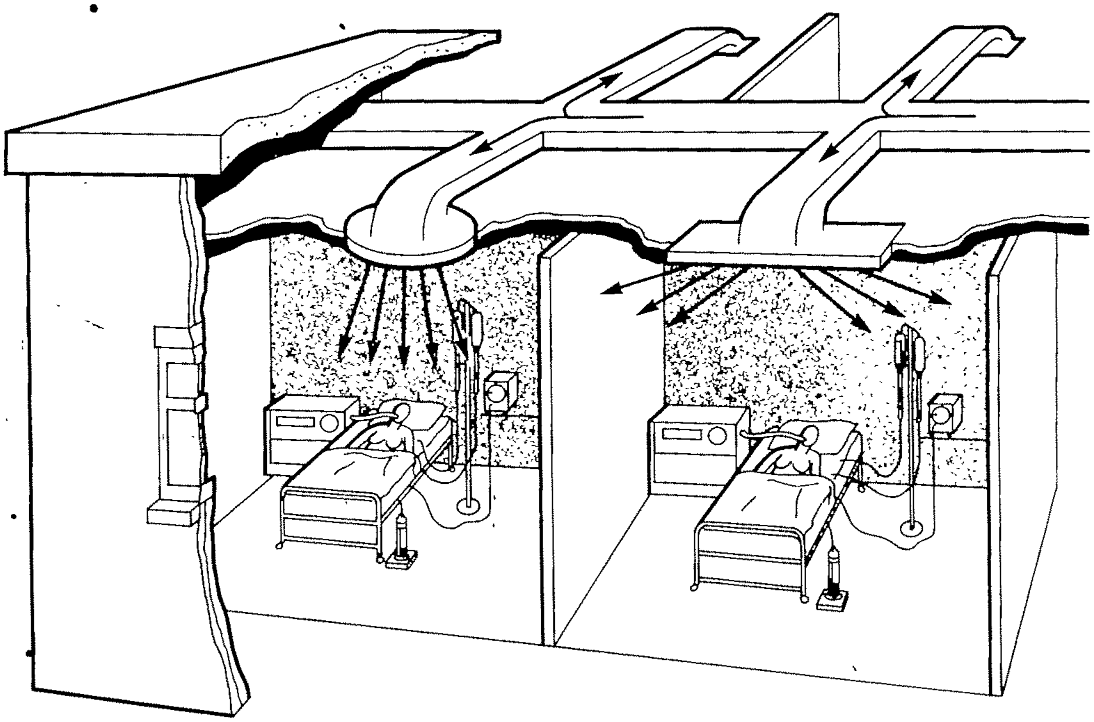


Fig. 1. Diagrammatic representation of a room with a direct down draught of incoming air and how this can and should be prevented by an inlet that gives a horizontal direction to the air flow.

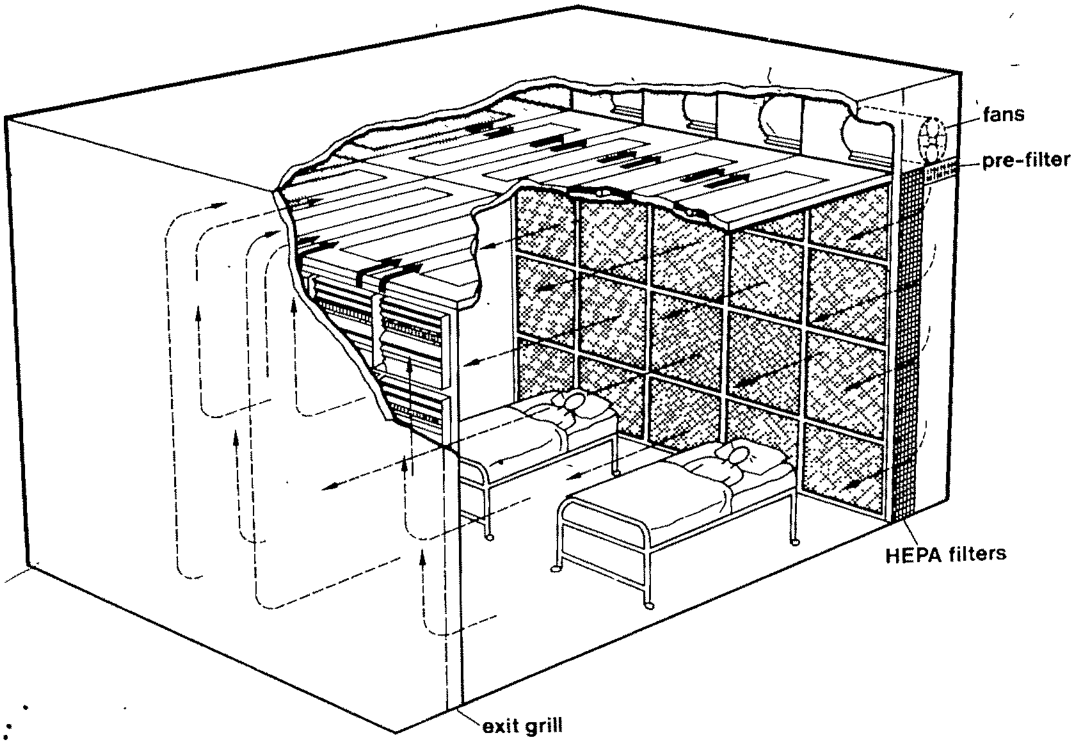


Fig. 2. Diagram showing a room air-conditioned by horizontal laminar flow.

The method that should be especially considered in the intensive care unit is laminar flow. This can be vertical or horizontal but the horizontal flow is likely to be more practical. This is possibly the best means of air-conditioning the intensive care unit (*Fig.* 2). The availability of commercial equipment designed for clean air industrial rooms means that the experience and production methods are available and that the cost need not be excessive. Careful thought should be given to the provision of laminar flow equipment. Many problems may be avoided if early thought is given to its provision while designing or modifying rooms and extra care in design can avoid any undue noise if the fans and humidifiers are carefully sited.

Acknowledgements

I wish to acknowledge the great help that I have received from Miss P. Archer and Mr Patrick Elliott of the Department of Medical Illustration at Guy's Hospital for their preparation of the two illustrations.

References

CLARK R. E. and RAVENSTINE E. A. (1954) Body temperature studies in anaesthetised man. *JAMA* **154**, 311–319.

HEALTH AND SOCIAL SERVICE JOURNAL (1974) Intensive care. Pp. 14, 37, 58.

IBSEN B. (1967) Treatment of shock with vasodilators measuring skin temperature. *Dis. Chest* **52**, 425–429.

MEDICAL RESEARCH COUNCIL AND DEPARTMENT OF HEALTH (1972) *Report by Joint Working Party on Ventilation in Operation Suites.* London, MRC and DHHS.

MINISTRY OF HEALTH (1967, reprinted 1972) *Hospital Building Note No. 26; The Operating Department.* London, HMSO.

MORRIS R. H. (1971) Influence of ambient temperature on patient temperature during abdominal surgery. *Ann. Surg.* **173**, 230–233.

MORRIS R. H. and WILKEY B. R. (1970) The effects of ambient temperature during surgery not involving body cavities. *Anaesthesiology* **31**, 102–107.

ROSS B. A., BROCK, LORD and AYNSLEY-GREEN A. (1969) Observations on central and peripheral temperatures in the understanding and management of shock. *Br. J. Surg.* **56**, 877–882.

ROYAL AIR FORCE INSTITUTE OF HEALTH AND MEDICAL TRAINING (1972a) Report IMHT No. 19/72. *An Environmental Survey of the Operating Suite at Wegberg.*

ROYAL AIR FORCE INSTITUTE OF HEALTH AND MEDICAL TRAINING (1972b) Report IMHT No. 27/72. *An Environmental Survey of the Operating Suite at Cambridge Military Hospital, Aldershot.*

ROYAL COLLEGE OF SURGEONS OF ENGLAND (1964) Report on design of operating theatre suites. *Ann. R. Coll. Surg. Engl.* **34**, 217–288.

SPITZER A. G. and BROCK, LORD (1968) The recognition of hypovolaemia after open heart surgery. *Guy's Hosp. Rep.* **117**, 131–138.

VERNER I. R. (1974) The organization, design and staffing of intensive therapy units. *Br. J. Hosp. Med.* **11**, 828–830.

WALKER W. F. (1973) Surgical intensive care. *Ann. R. Coll. Surg. Engl.* **53**, 50–56.

WYON D. P., LIDWELL O. M. and WILLIAMS R. E. O. (1968) Thermal comfort during surgical operations. *J. Hyg.* (*Camb.*) **66**, 229–248.

Br. J. Surg. Vol. 62 (1975) 259–263

Some observations on peripheral venous pressure using a non-invasive technique: a preliminary report

H. GAYLIS*

SUMMARY

Observations are presented which suggest that peripheral venous pressure can be measured indirectly by a non-invasive technique at the bedside, using a portable Doppler ultrasound flowmeter.

The pressure at which the audio signals are heard over veins on release of the occluding cuff seems to be a measure of peripheral venous pressure. This is supported by showing a correlation between the method and conditions in which raised venous pressure in the lower limb are known to exist. The results of a few direct venous pressure measurements are reported which appear to give added support.

It is suggested that this simple non-invasive technique may be of value in detecting certain cases of deep vein thrombosis of the lower extremities.

WHILE arterial blood pressure can be accurately measured by non-invasive techniques, such as sphygmomanometry, oscillometry and the Doppler ultrasound flowmeter, venous pressure can only be reliably measured by cannulation or puncture of veins, using a vertical saline manometer, aneroid manometer or strain gauge transducer. The measurement of venous pressure by a non-invasive technique could have great value in the diagnosis of certain diseases such as venous thrombosis. The purpose of this paper is to present a number of observations which suggest that peripheral venous pressure may be measured indirectly by non-invasive technique at the bedside, using a portable Doppler ultrasound flowmeter.

Materials and methods

A Doppler probe of a 10-MHz flowmeter is placed over the posterior tibial artery behind the medial malleolus (*Fig.* 1). Because the posterior tibial veins usually lie adjacent to the artery the Doppler probe will detect blood velocity changes in both the artery and the vein. An inflatable cuff just above the ankle is inflated to above systolic pressure. The cuff is slowly deflated at a rate of about 5 mm Hg per second. At first the characteristic arterial audio signals in phase with the cardiac cycle are heard. On further deflating the cuff, a superimposed continuous sound is audible at an average cuff pressure of about 30 mm Hg which disappears or fades at pressures varying between 10 and 0 mm Hg. *Fig.* 2 is a recording of the audio signals heard over the posterior tibial artery and vein at the ankle, as displayed on an oscilloscope with a storage memory. The recording was photographed with a Polaroid camera. At *A* the normal arterial audio signals corresponding with each pulse beat can be noted. At *B*, with the cuff inflated above systolic pressure, no flow signals can be seen, thus indicating cessation of

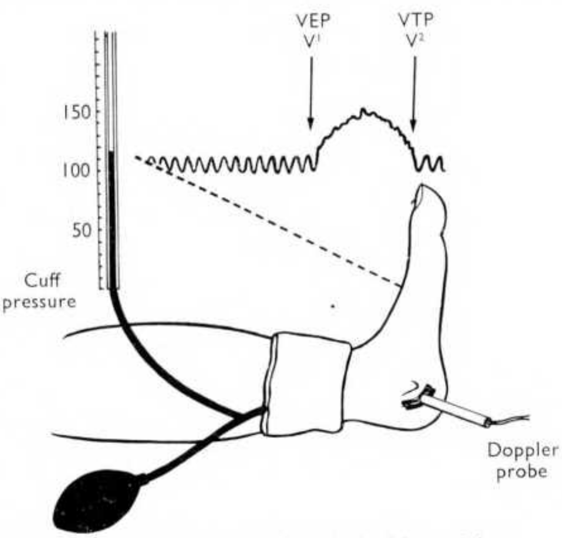


Fig. 1. Diagram to illustrate the method of determining peripheral venous pressures. *VEP* (V^1), Venous escape pressure. *VEP* (V^2), Venous terminal pressure.

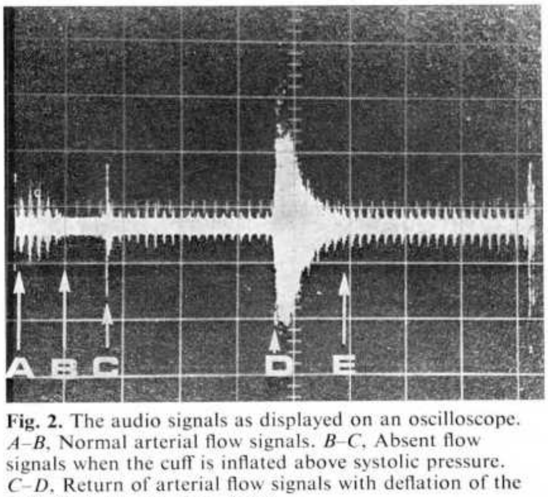


Fig. 2. The audio signals as displayed on an oscilloscope. *A–B*, Normal arterial flow signals. *B–C*, Absent flow signals when the cuff is inflated above systolic pressure. *C–D*, Return of arterial flow signals with deflation of the cuff. *D–E*, Venous flow signal.

---

* Department of Surgery, University of Witwatersrand and the General Hospital, Johannesburg.

arterial blood flow. At *C*, with the cuff pressure deflated below systolic arterial pressure, audio signals in phase with arterial pulsation reappear. As the cuff is further deflated, another signal (*D*) is seen which rapidly reaches a crescendo and, on further deflating the cuff, disappears at a cuff pressure of approximately 10 mm Hg.

That the onset of this second sound was caused by escape of venous blood under increased pressure behind the cuff is the likely explanation of the phenomenon. This is supported by the following observations. The posterior tibial veins accompany the posterior tibial artery and not infrequently 'S' sounds (spontaneous flow signals in phase with respiration) are audible in this region. 'A' sounds (augmented signals) can also be produced quite readily by sharp pressure on the soft tissues proximal to this region or by compression of the forefoot. Audio signals can also be heard by placing the probe over other visible veins on the dorsum of the foot such as the saphenous or anterior tibial veins. Futhermore, reversal of flow, coinciding with the venous audio signal, was confirmed with the directional Doppler.

Not only did it seem that the onset of the 'venous' audio signal coincided with the escape of venous blood behind the cuff, but it also seemed possible that the disappearance or attenuation of the venous sound was caused by equalization of venous pressure and thus venous velocity flow proximal and distal to the cuff. It thus seemed that the cuff pressure at which the venous audio signal disappeared or became attenuated could be a measure of peripheral venous pressure. If the supposition was correct then the method could clearly have value as a non-invasive technique of measuring peripheral venous pressure and that it could be of use in the diagnosis of some cases of deep vein thrombosis of the extremities.

To determine whether the disappearance of the 'venous' signal was an index of peripheral venous pressure, normal values would have to be established and then the method would have to be tested in limbs known to have an increase in venous pressure.

1. *Normal 'venous' cuff pressures*

Fifty patients who had no clinical evidence of venous or arterial disease of the lower extremities had both lower limbs evaluated. The patients lay supine with the head raised on one flat pillow. The reference level, considered as the right atrium, was chosen as a point half the anteroposterior diameter of the chest at the middle of the sternum. The vein under test, the posterior tibial vein at the medial malleolus of the ankle, was placed at the same level as this reference plane. The temperature and humidity of the room were not controlled. The Doppler ultrasound flowmeter used in the experiment was a Parks Model 802 or 803 (10 MHz) and the probes were either of the pencil or flat type. The rate of deflation of the collecting cuff was not accurately controlled but was approximately that used in deflating a cuff for determining normal blood pressure, i.e. ±5 mm/second.

Table I: ANKLE CUFF PRESSURES AT WHICH V^1 AND V^2 AUDIO SIGNALS WERE AUDIBLE IN 100 NORMAL LIMBS

	V^1 (mm Hg)		V^2 (mm Hg	
	R	L	R	L
No.	50	50	50	5
Mean	30	31	9	
Standard deviation	14	12	4	
Standard error	2	2	6	

R, Right. L, Left.

Table II: ANKLE CUFF PRESSURES V^1 AND V^2 ON VARYING THE PRESSURE ON THE COLLECTING CUFF ON THE CALF

Calf (mm Hg)	Ankle (mm Hg)											
	Case 1		*Case* 2		*Case* 3		*Case* 4		*Case* 5		*Case*	
	V^1	V^2	V^1	V^2	V^1	V^2	V^1	V^2	V^1	V^2	V^1	V
100	60	45	55	40	40	20	55	30	60	40	60	4
80	60	35	55	30	40	20	60	40	60	40	60	2
60	60	30	45	30	30	15	50	30	60	40	60	3
40	55	30	45	20	30	15	50	20	70	35	40	2
20	50	20	30	15	30	10	40	15	50	30	40	1
0	40	5	20	10	30	10	20	15	35	5	35	

The onset of the venous audio signal V^1 (venou escape pressure) and the disappearance of the venou audio signal V^2 (venous terminal pressure) wer recorded to the nearest 5 mm Hg. *Table I* shows th relevant data in each series of limbs and, as can b seen, the average V^1 pressure is about 30 mm Hg an the average V^2 pressure about 9 mm Hg. Eight patient had arterial hypertension but in this group there wa no increase in these two values. Whereas the V^1 pressures varied, the variation depending mainly on th rate of deflation of the collecting cuff, the V^2 pressure remained more constant. Furthermore, there wa good correlation between the values obtained in eac pair of limbs.

2. *The response to induced venous obstruction*

A collecting cuff was placed around the upper calf i 6 patients and various degrees of venous occlusio produced distally by varying the pressure of the cal cuff. The V^1 and V^2 cuff pressures were then recorde at the ankle at calf pressures varying from 0 t 100 mm Hg. *Table II* shows the V^1 and V^2 pressure relative to the calf pressures, and *Fig.* 3 a graphi representation of the data, but recording only the V pressures. As can be seen, the V^2 cuff pressure correlate with the different degrees of venous obstruction produced by the calf collecting cuff.

3. *Deep vein thrombosis*

The pressures at which the V^1 and V^2 signals are hear were recorded in 11 patients suffering from deep vei thrombosis in the upper and lower extremities. In patients the deep veins of one or both lower extrem ties were affected and in 2 patients the axillary sub clavian segments were occluded. The diagnosis wa made on clinical grounds alone, except in one patie who had in addition confirmatory venograph evidence. In 8 of the 11 patients tested the 'venou pressures were elevated (*Table III*).

Table III: V^1 AND V^2 CUFF PRESSURES IN 11 PATIENTS WITH CLINICAL DEEP VEIN OBSTRUCTION

Patient	Clinical diagnosis	Right V^1	Right V^2	Left V^1	Left V^2
E. M. R.	Left calf vein thrombosis	30	10	40	20
E. P.	Left axillary vein thrombosis	50	5	80	20
D. van D.	Left axillary vein thrombosis	45	10	55	15
R. W.	Bilateral femoral vein thrombosis	90	10	90	10
J. D.	Left femoral vein thrombosis	20	0	45	10
J. B.	Left axillary vein thrombosis	25	0	40	10
E. C.	Bilateral femoral vein thrombosis	60	20	55	20
E. L.	Left femoral vein thrombosis	35	5	30	15
W. R.	Left iliac vein thrombosis	15	5	40	20
A. K.	Bilateral femoral vein thrombosis	65	20	45	20
J. L.	Left iliac vein thrombosis	25	10	40	20

Table IV: DIRECT VENOUS PRESSURE RECORDINGS IN 4 PATIENTS COMPARED WITH V^2 PRESSURE

Case no.	Calf pressure (mm Hg)	Direct venous pressure (mm Hg)	Venous terminal (V^2) pressure (mm Hg)
1		7	5
2		4	5
3	0	9	5
	20	19	20
	60	38	35
4	0	4	5
	60	29	30

In *Cases* 3 and 4 a collecting cuff was applied and inflated to the levels recorded.

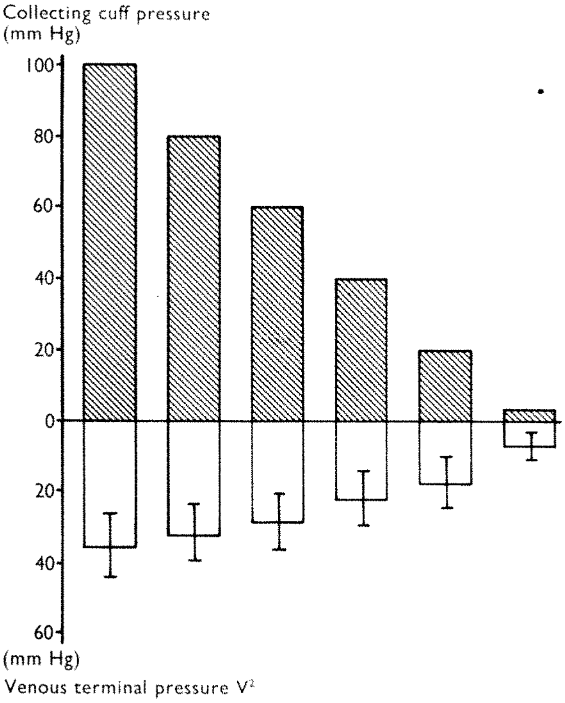


Fig. 3. Correlation between the V^2 pressures and the collecting cuff pressure. Each vertical bar represents the mean of 6 patients.

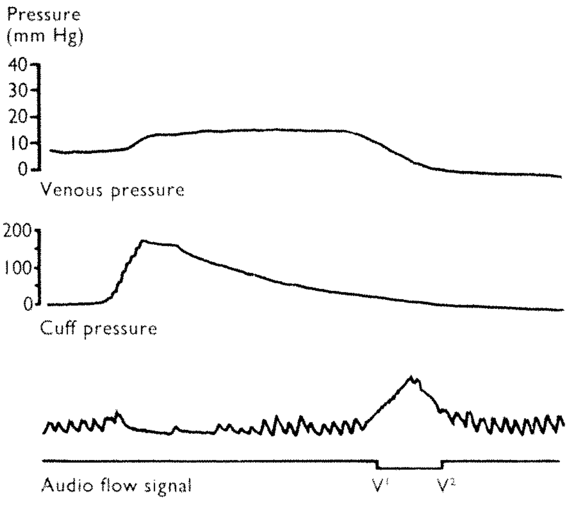


Fig. 4. Simultaneous instantaneous recordings of direct venous pressure, cuff pressure, flow signals and audio venous signals V^1 and V^2 as recorded by the observer. Note that the V^1 and V^2 observer audio signals correspond with the venous flow signal and with the venous escape and venous terminal pressures.

4. *Direct venous pressure measurements*

In 4 patients the venous cuff pressures (V^2) were correlated with venous pressures recorded by direct vertical saline manometry. The pressures were measured in a vein on the dorsum of the foot with the patient in the supine position. The resting venous pressures correlated fairly well with the V^2 pressures, and on increasing the peripheral venous pressure by inflating the collecting cuff on the calf there was a rise in peripheral venous pressure which corresponded fairly well with the V^2 signals (*Table IV*).

5. *Simultaneous instantaneous recordings*

In 3 patients simultaneous instantaneous recordings were made of the four relevant parameters. The patients were tested in the supine position and the parameters recorded were the direct intravenous pressure, the ankle cuff pressure, the arterial and venous flow signals and the onset and disappearance of the venous audio signal as heard by the observer. The pressures were measured by strain gauge transducers and the audio signal recorded on a DC recorder with a deflection factor of 50 MV/CM. The apparatus used to record the above parameters was a Beckman Dynagraph Recorder (Type RM). The venous pressures were recorded through a needle or cannula inserted into a vein on the dorsum of the foot.

Fig. 4 shows an average recording of the parameters investigated. As the cuff pressure is increased by the manually inflated cuff, there is a corresponding rise in venous pressure. When the cuff pressure rises above systolic arterial pressure, all flow signals disappear. On release of the cuff pressure, arterial flow signals in phase with the arterial pulse are clearly seen. The venous pressure now begins to increase and when the pressure distal to the cuff exceeds the cuff pressure, venous blood escapes and this is accompanied by the appearance of the escape flow signal (V^1) which is a high frequency continuous signal. As the venous pressure decreases and becomes static, the venous audio signal V^2 disappears to be replaced by normal arterial signals. The onset and disappearance of the venous audio signal as heard by an observer are seen to coincide with the flow signal and the changes in venous pressure.

Discussion

When an inflatable cuff which has been pumped above systolic pressure is deflated, arterial blood enters the part distal to the cuff when the systolic pressure exceeds the cuff pressure. If the cuff is not completely deflated the part distal to the cuff becomes distended with venous blood until the venous blood pressure exceeds the cuff pressure and blood begins to escape. The velocity of this escaping venous blood just behind the cuff is therefore increased and this change effectively accounts for the onset of the venous audio signal (V^1). As the venous pressure decreases on further deflating the cuff, the velocity flow presumably also decreases, and when the pressure behind the cuff returns to normal, the velocity flow reaches a steady state. This accounts for the disappearance of the venous signal (V^2), and the cuff pressure at which this occurs should signify the approximate peripheral venous pressure.

The supposition that the V^2 signal is an index of peripheral venous pressure is supported by the clinical results of this investigation and more importantly by direct venous pressure tracings. With regard to the clinical evidence the mean V^2 pressure in 100 normal limbs was 9 mm Hg (s.d. ± 4), and in each pair of limbs the correlation was good. These mean pressures correlate with direct venous pressures measured by others in unrelated studies. Winsor and Burch (1946) and Ochsner et al. (1951), in a study of venous pressures in peripheral veins, reported mean pressures of 150 mm H_2O (11·02 mm Hg) and 126 mm H_2O (9·26 mm Hg) respectively at the great saphenous vein at the ankle.

The correlation between the V^2 pressures and the graded increases in venous hypertension produced by varying the pressure of the calf collecting cuff (*Table II* and *Fig.* 3) is also further evidence supporting the hypothesis that the method is a measure of peripheral venous pressure. Further clinical support seems to be afforded by the few cases of deep vein thrombosis studied so far. In 8 of the 11 patients the V^2 cuff pressure was increased.

The correlation between the V^2 venous signals and the direct venous pressure readings (*Table IV*) and between the instantaneous simultaneous recordings of the direct venous pressures, cuff pressures and audio flow signals (*Fig.* 4) is good supportive evidence that the V^2 audio signal is an index of peripheral venous pressure.

The venous escape pressure V^1, however, does not always correlate with direct venous pressure, and the venous pressure may continue to rise after the onset of the signal as was shown in several recordings. This is understandable, considering that on deflating the cuff the arterial input may be greater than the venous outflow. Thus the V^1 audio signal simply indicates that venous blood is escaping past the cuff and that it is not necessarily a measure of the venous pressure at that point in time. Another observation of interest was that in some of the tracings the venous pressure, after deflation, fell below the venous pressure baseline before the cuff was inflated. It is thought that this phenomenon was the result of vasodilatation of veins caused either by mechanical distension of veins or by an accumulation of metabolites during the short period of circulatory arrest by the cuff.

With regard to the direct venous measurements, these were all done in superficial veins on the dorsum of the foot, whereas the venous signals were recorded over the posterior tibial veins which belong to the deep venous system. Objection may therefore be made to these two comparisons, but it is difficult to conceive of two different pressure systems in the superficial and deep systems, having regard to the abundant communications between the superficial and the deep system of veins. The exception, of course, would be where there was spasm of the superficial veins, when the pressure of these would fall to zero. Fegan (1967) stated that the deep and superficial pressures are equal in the resting limb in the erect subject.

Although the evidence strongly suggests a relatively good correlation between the V^2 audio signal and venous pressure, it should not be assumed that the cuff pressure at which the V^2 signal is heard is an accurate reflection of direct venous pressure. The susceptibility of veins, especially superficial veins, to change their dimension and cross-sectional area make the reliable measurement of venous pressure, velocity and volume very difficult. The mere introduction of a needle or cannula into superficial veins often causes spasm, which was frequently noted in these experiments. Moderate environmental changes and psychological factors have the same influence.

One of the difficulties with the cuff method in the normal supine position is that the disappearance of the audio signal is not always clear-cut and is subject to an observer error of ± 5 mm Hg. Further, in some cases the end-point was not at all determinable because the sound did not disappear even at cuff pressures of zero. However, when venous hypertension was induced by the application of a collecting cuff, the V^2 audio signals were more often discernible. The inability to discern the V^2 signal in some patients was probably related to a high venous flow in the resting state and this was often observed in patients with vasodilated extremities and also in those who had had a sympathectomy. Whereas the V^1 audio signal could be varied by altering the rate of cuff deflection, the V^2 audio signal was not subject to the same variation. This variation in V^1 cuff pressures on altering the state of deflation is understandable, considering that a greater volume of venous blood is allowed to accumulate when the rate of deflation is slowed.

All the venous audio signals in this experiment were recorded over the posterior tibial veins because venous signals were more readily detected here than over other veins on the dorsum of the foot. Venous signals are detectable over the long saphenous and other veins on the dorsum, but these are more prone to go into spasm. When venous signals are recorded over the long saphenous vein at the medial malleolus, however, the V^1 and V^2 audio signals usually correspond with those obtained over the posterior tibial veins. In some cases where they did not correspond this was thought to be due to a difference in the cuff pressure required to compress the two different system of veins. The long saphenous vein is subcutaneous and lies on bone and therefore less pressure is required to compress it than the more deeply situated posterior tibial veins, which lie protected under the deep fascia.

An interesting feature on deflating the ankle cuff was the occasional observation of an 'audio gap', reminiscent of the auscultatory gap noted on recording arterial blood pressure. It was thought at first that this was an artefact caused by the cuff in which part of the cuff was fully deflated. However, this audio gap could not be abolished by altering the position or the type of the cuff. This anomaly remains unexplained at present.

In about 15 per cent of limbs the venous audio signals could not be heard over the posterior tibial veins. The reasons for this are open to speculation and could be accounted for by some anatomical anomaly, by occlusion by previous venous thrombosis or by too great a depth of the vein from the skin and thus from the probe.

With regard to positioning the probe over the vein it is essential that no undue pressure be produced. This may cause narrowing of the vein which could alter the velocity flow to give false values. Accordingly the probes were lightly positioned over the vein, and in the instantaneous simultaneous recordings of audio signals, flat probes were used which were lightly placed on the skin with coupling gel and the probe held in position with adhesive tape.

In conclusion it would appear that this non-invasive technique of assessing peripheral venous pressure using the Doppler ultrasound flowmeter may be of value in screening patients suspected of suffering from deep vein thrombosis. Although it has not been shown that the values obtained with this technique are absolute, there appears to be relatively good correlation. The technique may be of value for detecting certain cases of deep vein thrombosis, but it could obviously not detect all, having regard to the fact that deep vein thrombosis may exist, without increased venous pressure, for example where the thrombus is of the non-occlusive type or where the collateral circulation is good. A trial is now in progress to assess further the possibilities of this interesting observation.

Acknowledgements

I am grateful to Professor D. J. du Plessis for his encouragement and comments and to Mr C. D. Bremner for his technical assistance with recordings.

References

FEGAN G. (1967) *Varicose Veins*. London, Heinemann, p. 31.

OCHSNER A., COLP R. and BURCH G. E. (1951) Normal blood pressure in the superficial venous system of man at rest in the supine position. *Circulation* **3**, 674–680.

WINSOR T. and BURCH G. E. (1946) Use of phlebomanometer: normal venous pressure values and a study of certain clinical aspects of venous hypertension in man. *Am. Heart J.* **31**, 387–406.

Br. J. Surg. Vol. 62 (1975) 264–268

Report of a family with inherited medullary carcinoma of the thyroid and phaeochromocytoma

J. M. BEAUGIE, P. E. BELCHETZ, C. L. BROWN, R. J. FRANKEL
AND MARGARET H. LLOYD*

SUMMARY

A family in which several members have medullary carcinoma and phaeochromocytoma is described. Four of the 5 patients in this family who had a phaeochromocytoma have died; in one of these the medullary carcinoma may have contributed to death but in general the thyroid cancers were slow growing. In our experience successful diagnosis and treatment of the phaeochromocytomas have presented the greatest challenge. The welfare of future generations with this syndrome would seem to depend upon regular clinical and biochemical surveillance of the individuals and expeditious diagnosis and treatment of their tumours, particularly the phaeochromocytomas.

THE association of medullary carcinoma of the thyroid with phaeochromocytoma of the adrenal constitutes a well-known familial syndrome (Sipple, 1961; Williams, 1965; Williams et al., 1966; Block et al., 1968; Williams, 1970; Melvin et al., 1971; Keiser et al., 1973) inherited through an autosomal dominant gene (Steiner et al., 1968). The disease is therefore seen in either sex and is likely to manifest itself in half the offspring of an affected individual (Keiser et al., 1973). The tumours in the thyroid and adrenal are often bilateral and multiple, and other stigmata of the syndrome include neuromatous malformations at mucocutaneous junctions (Williams and Pollock, 1966) and parathyroid hyperplasia or adenoma (Gorlin and Mirkin, 1972; Keiser et al., 1973). These tumours have been grouped together forming the syndrome 'multiple endocrine neoplasia or adenopathy type II' (Steiner et al., 1968), in contrast to the tumours of 'multiple endocrine neoplasia type I' which includes the parathyroid, pancreatic and anterior pituitary adenomas associated with peptic ulcers (Wermer, 1954, 1963).

Medullary carcinoma is a malignant tumour of the parafollicular or 'C' cell of the thyroid (Williams, 1966a). The parafollicular cell appears to migrate from the neural crest in the embryo (Pearse, 1966); it secretes calcitonin (Foster et al., 1964) and is a so-called 'APUD' cell because it is able to concentrate and decarboxylate amine precursors (Pearse and Welbourn, 1973). Medullary carcinoma regularly secretes calcitonin and may also secrete adrenocorticotrophic hormone (Williams, Morales and Horn, 1968), prostaglandins (Williams, Karin and Sandler, 1968), serotonin (5-hydroxytryptamine) (Moertel et al. 1965) and histaminase (Baylin et al., 1970). Nearly one-third of the patients suffer from diarrhoea, perhaps due to one or more of these hormones
chemical substances (Williams, 1966b).

In this paper we present some cases of the famili
syndrome seen at The London Hospital. There are,
course, other and larger families in the world liter
ture (for example, Block et al., 1968; Steiner et al
1968; Melvin et al., 1971; Keiser et al., 1973). O
family is perhaps the largest and most complete wi
a high degree of penetrance of the gene to be report
in Great Britain. The most difficult problem h
proved to be the diagnosis and treatment of th
phaeochromocytomas which will therefore be co
sidered in some detail.

Biochemical assay methods

Vanillylmandelic acid (VMA) was estimated in uri
collected over 24 hours into a bottle containing 1
15 ml of concentrated hydrochloric acid and assay
by a modification of Pisano's method (Connelian a
Godfrey, 1964). The normal range is 3–8 mg/24 hou
Other urinary catecholamine metabolites we
measured semi-quantitively by two-dimensional pap
chromatography (Robinson and Smith, 1962). Calcit
nin in plasma and tissue was measured by Professor
McIntyre using a specific radio-immunoassay. T
normal value for plasma calcitonin is less th
0·5 ng/ml and for normal thyroid less than 1 ng/
Adrenocorticotrophic hormone (ACTH) in plas
and tissue was measured by Dr J. G. Ratcliffe usi
N-terminal specific antibody radio-immunoassay aft
extraction with porous glass (Ratcliffe and Edwar
1971). Normal plasma ACTH is less than 70 pg/ml.

Members of the family studied

Two generations of the family are known to
affected by medullary carcinoma with phaeochrom
cytoma (*Fig.* 1). The father (H. B. sen.) had 6 childr
of whom all except the youngest have had at least o
type of tumour. There are 9 children in the thi
generation who are under the age of 18 years and o
has a goitre, but since she is mentally subnormal it h
not been possible to investigate her. No clinical
biochemical evidence of medullary carcinoma
phaeochromocytoma has been found so far in t
other 8 children.

---

* Departments of Medicine and Surgery, and the Institute
Pathology, The London Hospital, London.
Present address of P. E. Belchetz: Northwick Park Hospi
Harrow, Middlesex.
Present address of R. J. Frankel: St George's Hospi
London.

H. B. sen. died suddenly at home aged 67 years. At a coroner's autopsy bilateral phaeochromocytomas were found and confirmed histologically. The state of his thyroid was not reported.

E. S., his eldest daughter, died suddenly at another hospital aged 46 years. The post-mortem revealed carcinoma of the thyroid with pulmonary and adrenal metastases. This diagnosis is unconfirmed histologically but, considering her family background, she probably had medullary carcinoma and bilateral phaeochromocytomas.

H. B. jun., the eldest son, died in The London Hospital aged 43 years. He was admitted from the Diabetic Clinic, which he had attended for many years, for investigation of hypertension. This included a phentolamine test which was positive, following which he developed profound hypotension and died. At post-mortem there were bilateral medullary carcinomas in the thyroid and bilateral phaeochromocytomas.

J. S., the second daughter, is alive aged 41 years. For at least 18 years she has had a swelling in the right lobe of the thyroid. There were no symptoms of phaeochromocytoma but her blood pressure was 170/110. The 24-hour ^{131}I thyroid uptake was 68 per cent (normal 34–55 per cent) and a scan showed non-functioning areas in both lobes. Her protein-bound iodine was normal and thyroid auto-immune microsomal antibodies were positive by the fluorescent technique. Her plasma calcitonin was 7·7 ng/ml. Investigations of her hypertension revealed a normal IVP and blood urea and no proteinuria. Repeated VMA levels were also normal.

A total thyroidectomy was performed (*Fig.* 2). The medullary carcinoma in the right lobe was 3·7 cm in diameter and that in the left 2·5 cm. There was some calcification in the tumours, marked lymphocytic infiltration in the thyroid parenchyma and microscopic foci of medullary carcinoma near the main tumours. The tumour calcitonin level was 10 000 ng/mg. She is now in good health, without evidence of thyroid cancer or phaeochromocytoma. Her blood pressure 3 years after thyroidectomy is 170/85 mm Hg and VMA excretion is within normal limits.

A. B., the second son, died at the age of 38 years. He had a solitary nodule in the right inferior pole of his thyroid of which he was not aware, and for 6 years had suffered the symptoms of phaeochromocytoma. A ^{131}I thyroid scan confirmed a cold nodule, and the plasma calcitonin level was 1 ng/ml. His blood pressure was 140/90–170/110 and the phaeochromocytoma was confirmed by 24-hour urinary VMA estimations of 8·4, 9·4 and 12·0 mg and excessive urinary levels of normetadrenaline and metadrenaline. The phenotolamine test was positive. The 24-hour urinary 17-oxogenic steroid level was 20·5 mg and 17-oxosteroid 14·2 mg (normal 7–20 mg and 5–20 mg respectively).

A. B.'s phaeochromocytomas were treated by bilateral adrenalectomy; first the left was removed at laparotomy, followed 2 weeks later by the right through a costophrenic approach. The right adrenal weighed 19·0 g and the left 5·5 g (normal weight up to 4·5 g). Apart from several phaeochromocytomas, there was a marked increase in compact cells of the cortex, signifying excessive ACTH stimulation (*Fig.* 3). Afterwards, the patient was clinically well, taking cortisone acetate 12·5 mg three times daily and fludrocortisone 0·1 mg daily, but the plasma ACTH was very high, being 335 pg/ml at 9.00 hours (normal 70 pg/ml) and 195 pg/ml at midnight.

Three months after adrenalectomy near total thyroidectomy was performed. The medullary carcinoma in the right lobe measured 3 cm in diameter and the left 0·5 cm (*Figs.* 2, 4). The tumour contained ACTH to a level of 0·1 pg/g of tissue, which is greater than in normal tissue (Rees, 1974).

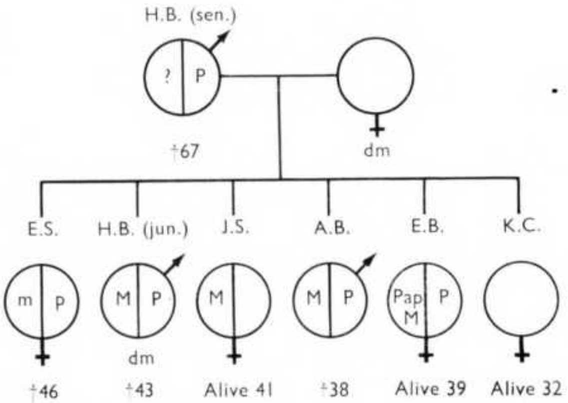


Fig. 1. Family tree. *M*, Proved medullary carcinoma. *P*, Proved phaeochromocytoma. *m*, Suspected medullary carcinoma. *p*, Suspected phaeochromocytoma. *dm*, Diabetes mellitus. *Pap.*, Papillary carcinoma.

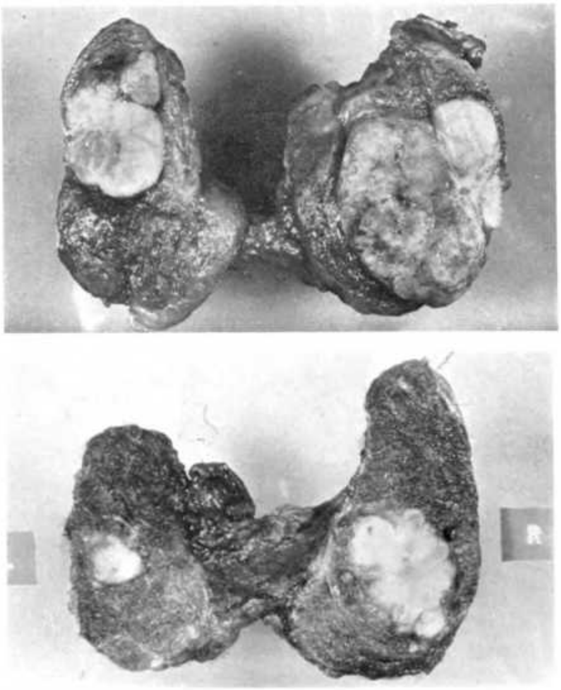


Fig. 2. Photographs of the thyroidectomy specimens from J. S. (*above*) and A. B. (*below*) showing the similarity in location of the main medullary carcinomas in both lateral lobes of the two glands.

Six months later A. B. developed Addisonian pigmentation even though his steroid replacement dose had been raised to 50 mg of cortisone acetate daily. His plasma ACTH level at that time was very high (890 pg/ml) but was suppressible by increasing doses of dexamethazone to 50 pg/ml when he took 16 mg of dexamethazone daily. These levels when the patient was apparently having adequate steroid replacement suggested the presence of ectopic ACTH-secreting tissue; a suggestion reinforced by the finding of an enlarged liver and a ^{198}Au liver scan with an abnormal uptake pattern. In the chest X-ray the left hemidiaphragm was raised.

His clinical condition was stable for 18 months before he died suddenly despite large doses of intravenous hydrocortisone. At autopsy there was no medullary carcinoma or other neoplasm in the liver which could have secreted ACTH but there was a large subphrenic abscess on the left side. The pituitary contained many 'shock' cells, suggesting that it had been secreting excessive quantities of ACTH. The acidophils were well granulated and the thyrotroph cells were normal, indicating that thyroid replacement therapy had been adequate.

E. B. is the third daughter now aged 39 years. She was 8 years old when a goitre was noticed and was eventually treated by subtotal thyroidectomy at the age of 16 years. The specimen

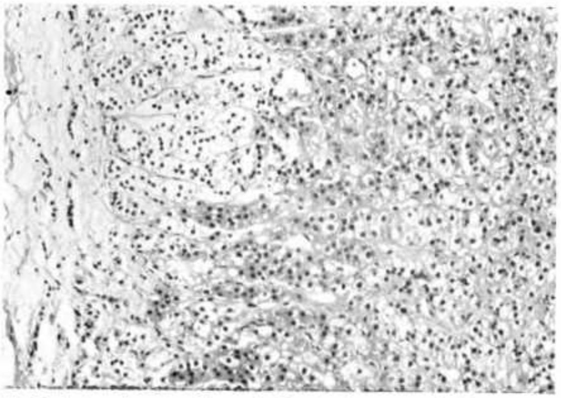


Fig. 3. Adrenal cortex from A. B. showing a marked increase in numbers of compact cells, in places forming columns extending out to the capsule. HE. (× 88.)

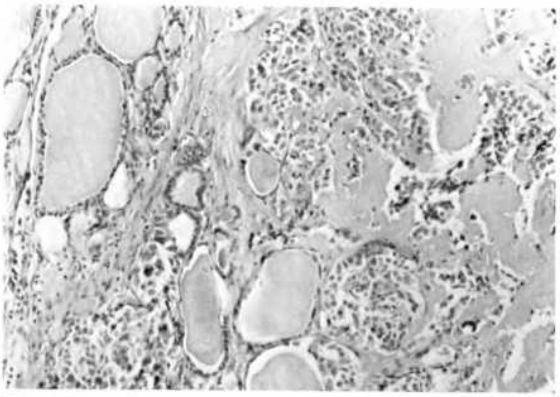


Fig. 4. Edge of tumour from A. B. showing uniform carcinoma cells separated by masses of amyloid and nvading surrounding thyroid follicles. HE. (× 88.)

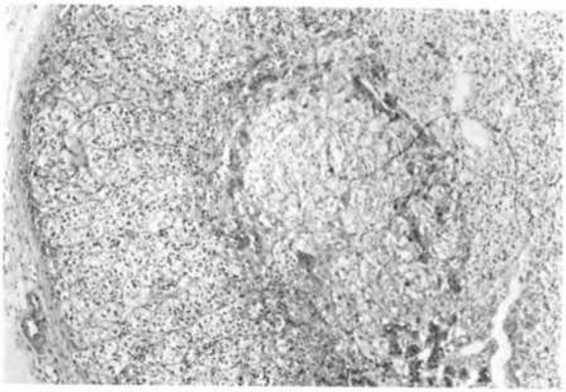


Fig. 5. Adrenal from E. B. which was macroscopically normal, but showing one of several microscopic phaeochromocytomas. HE. (× 41.)

contained a papillary carcinoma confined to the thyroid. During the next 12 years several metastatic lymph nodes were removed, culminating in bilateral dissections of the neck nodes 13 years ago. On further study this last specimen was found to contain not only papillary carcinoma but also multiple discrete nodules of medullary carcinoma in the thyroid remnant. Since then she has needed one further excision of a lymph node containing papillary carcinoma, but no further medullary carcinoma has been found.

E. B. had suffered the symptoms of phaeochromocytoma for 12 years and her blood pressure varied between 150/100 and 210/130. The diagnosis was confirmed by a 24-hour urinary VMA excretion of 29 mg and an excess of both normetadrenaline and metadrenaline in the urinary chromatogram. A phentolamine test was not done. She was treated by bilateral adrenalectomy; the right gland weighed 183 g and contained two phaeochromocytomas, and the left was normal in size and macroscopic appearance, but contained several microscopic tumours (*Fig.* 5). Following operation her blood pressure returned to normal and remains so 3 years later.

K. C. is the youngest daughter aged 32. She has no clinical or biochemical evidence of thyroid or adrenal disease.

Discussion

This family shows a very high incidence of medullary carcinomas and phaeochromocytomas when compared with some others (Steiner et al., 1968; Melvin et al., 1971; Keiser et al., 1973), but differs from them in having no recorded parathyroid abnormalities or mucosal neuromas. Our kindred found so far is small compared with the 256 known members of one family (Keiser et al., 1973) of which 44 were examined and found to suffer from 25 medullary carcinomas, 11 phaeochromocytomas and 16 parathyroid abnormalities with 6 of the patients having all three stigmata. This latter kindred is not regarded as complete and the members traced so far may be as little as one-quarter of the family at risk, leaving perhaps 130 affected but undetected living relatives. In another large kindred (Steiner et al., 1968) 186 members were found to suffer from 5 medullary carcinomas, 10 proved and 15 probable phaeochromocytomas and 2 cases of parathyroid hyperplasia. Searching a kindred for new cases, therefore, is likely to be rewarding but the proportion of positive results does vary from family to family. The first member of the family to come to light is perhaps the most unfortunate because his doctors will not be so aware of the possible abnormalities as when seeing subsequent members. In our family H. B. jun. was the first to be seen by us and he died following a phentolamine test before he was recognized as a familial case; both members of the family who died beforehand elsewhere were not suspected of having a familial disease. In our family, therefore, 3 members died before the familial nature of the condition was recognized.

Any patient who presents with a thyroid nodule which is suspicious of carcinoma and particularly one which is thought or proved to be a medullary carcinoma must be screened for hypertension and asked for a family history of thyroid and adrenal operations and cases of sudden death. Any new patient with a phaeochromocytoma should be asked the same questions. Once the clinical diagnosis has been made it should be confirmed not by the phentolamine test as in H. B. jun., who had a fatal reaction, but by an examination of urine for products of catecholamine metabolism. Provided that the urine is kept at a pH below 3 and sensitive chemical assay methods are used, a near 100 per cent diagnostic accuracy has been reported without false positive findings (Freier and Harrison, 1973). Also the phentolamine test may give false positive results in other hypertensive patients (Guazzi et al., 1973) and should only be performed with an intravenous infusion of physiological saline running to correct hypovolaemic hypotension.

Since phaeochromocytomas can be suddenly lethal they should be treated first (Keiser et al., 1973). Bilateral adrenalectomy is required because tumours are usually situated within both adrenal glands and may be of microscopic size. Localization of the tumours by special tests is probably unnecessary and may be dangerous, and the final arbitrator is usually the surgeon's fingers (DeQuattro, 1972). Adrenalectomy is safest when performed through a thoracophrenic incision with the patient placed in the lateral position, so that adrenal veins can be ligated before the tumour is disturbed, though some authors recommend a transabdominal approach (Keiser et al., 1973). Both adrenals can be explored in one session through two incisions if the patient is turned from one side to the other and the blood pressure stabilizes after repositioning. In A. B.'s case the first operation was left adrenalectomy through an epigastric midline incision and the fatal subphrenic abscess which occurred is perhaps more likely to follow this approach than the costophrenic route (Welbourn et al., 1971).

The medullary carcinomas in this family were slow growing in that 2 patients had a goitre for 13 and 18 years respectively and there is strong evidence of metastases in only 1 patient (E. S.). With the possible exception of E. B., tumours were bilateral, as expected, and could therefore only be treated by near total thyroidectomy (Keynes and Till, 1971; Keiser et al., 1973). The coincidence of metastasizing papillary carcinoma and medullary carcinoma found in E. B. must be very rare. This case was reported by Williams et al. (1966) as an example of sporadic medullary carcinoma with papillary carcinoma.

In view of the generally slow progress of the medullary thyroid carcinomas our mistaken diagnosis of liver metastases in A. B. 6 months after total thyroidectomy was premature. It was suggested by an abnormal appearance in the ^{198}Au liver scan and by high levels of circulating ACTH. Such liver scans should perhaps be interpreted with caution, and a high blood ACTH level is equally compatible with a secreting tumour or adrenal insufficiency. The positive dexamethazone suppression test done earlier supports this latter hypothesis. It is possible that the undetected abscess had triggered off a brisk pituitary ACTH output as the steroid dosage was inadequate in the face of infection. It is, nevertheless, likely that the primary tumour in the thyroid did secrete ACTH because there were high levels in the tissue, and the adrenal cortex seen histologically was very active.

The deaths in the family have resulted less from thyroid carcinoma than from three classic difficulties of phaeochromocytoma: failure to be aware that a patient may have the condition, an adverse reaction to phentolamine and a septic complication of adrenalectomy. By regular surveillance of members of the next generation every 1 or 2 years these risks to the family should lessen. Apart from clinical features the serum calcitonin and urinary VMA are the variables to be monitored and an abnormally high level of either might be an indication for removal of the appropriate organ. This course is recommended by Melvin et al. (1971) and Miller et al. (1972), who performed thyroidectomy on 11 patients in their kindred with raised serum calcitonin levels and always found medullary carcinoma.

Acknowledgements

We would like to thank Dr A. Stuart-Mason, Mr J. E. Richardson and Professor I. Doniach for permission to publish details of this family and Professor H. D. Ritchie for help with the manuscript.

References

BAYLIN S. B., BEAVEN M. A., ENGELMAN K. and SJOERDSMA A. (1970) Elevated histamine activity in medullary carcinoma of the thyroid gland. *New Engl. J. Med.* **283**, 1239–1244.

BLOCK M. A., MILLER J. M. and HORN R. C. (1968) Medullary carcinoma of the thyroid: surgical implications. *Arch. Surg.* **96**, 521–526.

CONNELIAN T. P. and GODFREY J. M. (1964) The routine determination of urinary 4-hydroxy-3 methoxymendelic acid. *Clin. Chim. Acta* **9**, 410–412.

DEQUATTRO V. (1972) Treatment of phaeochromocytoma—diagnosis and preparation for operation. *Calif. Med.* **117**, 56–62.

FOSTER G. V., MACINTYRE I. and PEARSE A. G. E. (1964) Calcitonin production and the mitochondrion-rich cells of the dog thyroid. *Nature (Lond.)* **203**, 1029–1030.

FREIER D. T. and HARRISON T. S. (1973) Rigorous biochemical criteria for the diagnosis of phaeochromocytoma. *J. Surg. Res.* **14**, 177–180.

GORLIN R. J. and MIRKIN B. L. (1972) Multiple mucosal neuromas, phaeochromocytoma, medullary carcinoma of the thyroid and Marfanoid body build with muscle wasting. *Z. Kinderheilkd.* **113**, 313–325.

GUAZZI M., FIORENTINI C., POLESE A. and MAGRINI F. (1973) Hemodynamic factors conditioning the hypotensive response to phentolamine. *Jap. Heart J.* **14**, 1–11.

KEISER H. R., BEAVEN M. A., DOPPMAN J., WELLS A. jun. and BUJA L. M. (1973) Sipple's syndrome: medullary thyroid carcinoma, and parathyroid disease. *Ann. Intern Med.* **78**, 561–579.

KEYNES W. M. and TILL A. S. (1971) Medullary carcinoma of the thyroid gland. *Q. J. Med.* **40**, 443–456.

MELVIN K. E. W., MILLER H. H. and TASHJIAN A. H. jun. (1971) Early diagnosis of medullary carcinoma of the thyroid gland by means of calcitonin assay. *New Engl. J. Med.* **285**, 1115–1120.

MILLER H. H., MELVIN K. E. W., GIBSON J. M. and TASHJIAN A. H. jun. (1972) Surgical approach to early familial medullary carcinoma of the thyroid. *Am. J. Surg.* **123**, 438–443.

MOERTAL C. G., BEAHRS O. H., WOOLNER L. B. and TYCE G. M. (1965) Malignant carcinoid syndrome associated with non-carcinoid tumours. *New Engl. J. Med.* **273**, 244–248.

PEARSE A. G. E. (1966) 5-Hydroxytryptophan uptake by dog thyroid 'C' cells, and its possible significance in polypeptide hormone production. *Nature (Lond.)* **211**, 598–600.

PEARSE A. G. E. and WELBOURN R. B. (1973) The apudomas. *Br. J. Hosp. Med.* **10**, 617–624.

RATCLIFFE J. G. and EDWARDS C. R. W. (1971) The extraction of adrenocorticotrophic and arginine-vasopressin from human plasma by porous glass. In: KIRKHAM K. E. and HUNTER W. M. (ed.) *Radioimmunoassay Methods: European Workshop.* Edinburgh, Livingstone, pp. 502–512.

REES L. (1974) Personal communication.

ROBINSON R. and SMITH P. (1962) Urinary amines in phaeochromocytoma. *Clin. Chim. Acta* **7**, 29–33.

SIPPLE J. H. (1961) The association of phaeochromocytoma with carcinoma of the thyroid gland. *Am. J. Med.* **31**, 163–166.

STEINER A. L., GOODMAN A. D. and POWERS S. R. (1968) Study of a kindred with phaeochromocytoma, medullary thyroid carcinoma, hyperparathyroidism and Cushing's disease: multiple endocrine neoplasia. *Medicine* **47**, 371–409.

WELBOURN R. B., MONTGOMERY D. A. D. and KENNEDY T. L. (1971) The natural history of treated Cushing's syndrome. *Br. J. Surg.* **58**, 1–16.

WERMER P. (1954) Genetic aspects of adenomatosis of endocrine glands. *Am. J. Med.* **16**, 363–371.

WERMER P. (1963) Endocrine adnomatosis and peptic ulcers in a large kindred. *Am. J. Med.* **35**, 205–212.

WILLIAMS E. D. (1965) A review of 17 cases of carcinoma of thyroid and phaeochromocytoma. *J. Clin. Pathol.* **18**, 288–292.

WILLIAMS E. D. (1966a) Histogenesis of medullary carcinoma of the thyroid. *J. Clin. Pathol.* **19**, 114–118.

WILLIAMS E. D. (1966b) Diarrhoea and thyroid carcinoma. *Proc. R. Soc. Med.* **50**, 602–603.

WILLIAMS E. D. (1970) Medullary carcinoma of the thyroid. In: TAYLOR S. and FOSTER G. (ed.) *Calcitonin 1969. Proceedings of the Second International Symposium.* London, Heinemann, pp. 438–486.

WILLIAMS E. D., BROWN C. L. and DONIACH I. (1966) Pathological and clinical findings in a series of 67 cases of medullary carcinoma of the thyroid. *J. Clin. Pathol.* **19**, 103–113.

WILLIAMS E. D., KARIN S. M. M. and SANDLER M. (1968) Prostaglandin secretion by medullary carcinoma of the thyroid: a possible cause of the associated diarrhoea. *Lancet* **1**, 22–23.

WILLIAMS E. D., MORALES A. M. and HORN R. C. (1968) Thyroid carcinoma and Cushing's syndrome: a report of two cases with a review of the common features of the 'non-endocrine' tumours associated with Cushing's syndrome. *J. Clin. Pathol.* **21**, 129–135.

WILLIAMS E. D. and POLLOCK D. J. (1966) Multiple mucosal neuromata with endocrine tumours: a syndrome allied to von Recklinghausen's disease. *J. Pathol. Bacteriol.* **91**, 71–80.

Br. J. Surg. Vol. 62 (1975) 269–274

Neoplastic change in duplications of the alimentary tract

M. M. ORR AND A. J. EDWARDS*

SUMMARY

Two cases of adenocarcinoma arising in sequestrated duplications of the bowel in adults are reported. The literature is reviewed and a tendency for duplications to present in early childhood is noted. Although relatively few of these anomalies persist into adult life 8 cases of neoplastic change have now been reported. The histological features of many of the duplications undergoing malignant degeneration suggest the presence of underlying epithelial instability in this condition. It is postulated that duplications of the large bowel have malignant potential.

DUPLICATIONS of the alimentary tract are spherical or tubular congenital anomalies lined by mucous membrane and, typically, well-developed smooth muscle layers. They may arise at any level from the mouth to the anus (Gross et al., 1952) and usually lie in the dorsal mesentery intimately attached to the bowel wall. The rarer tubular variety—under one-third of the total—often communicate with the bowel lumen. The small intestine is the most common segment of bowel involved. Of 242 reported cases (Lo Presti et al., 1949; Gross et al., 1952; Forshall, 1961), 70 per cent involved this site and 14 per cent were at oesophageal level. Duplications of the large bowel are relatively uncommon. However, in 19 exclusively adult cases reviewed by Nolan and Lee (1953) the distribution was more uniform. Generally, duplications produce complications such as intestinal obstruction or haemorrhage requiring surgical treatment in infancy or childhood (Ladd and Gross, 1940; Forshall, 1961), but they may present in adult life as a result of similar complications or as incidental findings at operations or autopsies.

Closed duplications tend to enlarge, as secretions from the mucosal lining accumulate, and cause obstruction of the related loop of bowel or, less commonly, mechanical interference with other structures. They may produce pain purely as a result of increased tension within the cyst, or show the typical clinical features of mesenteric cysts in general. Duplications communicating with the bowel lumen are more often complicated by haemorrhage or perforation, as a result of ischaemia or of peptic ulceration in an area of heterotopic gastric mucosa.

Neoplastic change in a duplication would seem to be a very uncommon event. Few cases have been reported in the literature (Willis, 1967) but most of them concern duplications of the large bowel. These cases have shown few other features in common because of the diversity of form and site displayed by the duplications. The purpose of this paper is to report 2 further cases of this condition and to draw attention to some important considerations regarding its incidence, aetiology and treatment.

Case reports

Case 1: Mrs A. F., a 57-year-old housewife and secretary, presented with a 5-day history of pain in the right lower abdomen, anorexia and mild constipation. The pain was a constant dull ache made worse by eating. There was no history of rectal bleeding or of urinary symptoms. On examination she was mildly pyrexial and there was a tender mass to the right of the umbilicus. The mass was about 10 cm in diameter, hard, rounded and fairly mobile. Pelvic examination was normal.

The patient was admitted immediately for full assessment. The positive findings were a leucocytosis of 15 400/mm^3 with

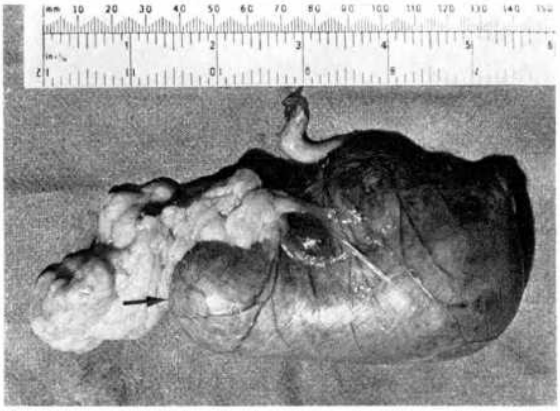


Fig. 1. *Case* 1. Tubular duplication excised from the transverse mesocolon, showing a vascular pedicle (above), diverticula and attached fat. Site of firm pale area of medial pole is arrowed.

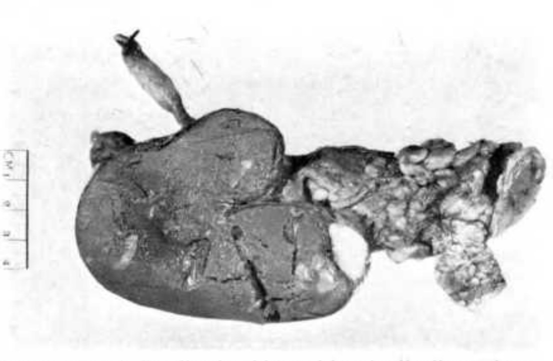


Fig. 2. *Case* 1. Duplication bisected longitudinally to show contained mucoid coagulum and pale nodule in the wall at the medial end.

---

* St Bartholomew's Hospital, London.

Requests for reprints to M. M. Orr, Surgical Professorial Unit, St Bartholomew's Hospital, London.

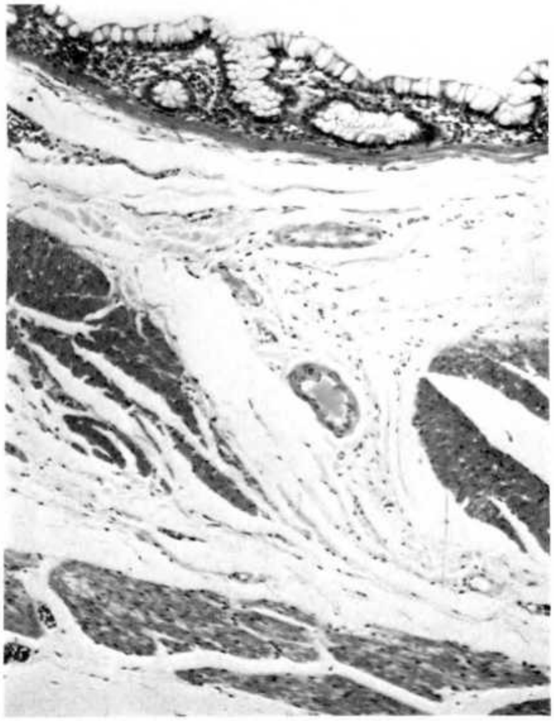


Fig. 3. *Case* 1. Section of the wall of the duplication showing mucous membrane, with mucus-secreting columnar epithelium, and double layer of smooth muscle. (× 100.)

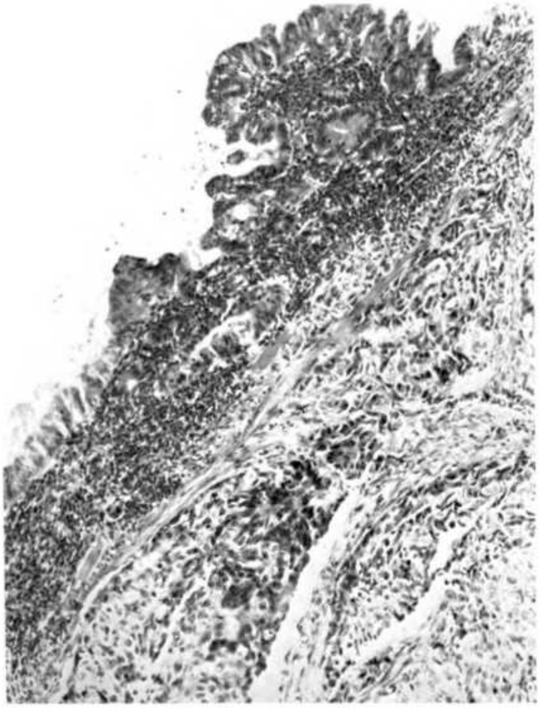


Fig. 4. *Case* 1. Poorly differentiated adenocarcinoma arising from mucous membrane and infiltrating wall of duplication. Note the abnormal epithelium to the left of the frank carcinoma, with cellular atypia and absence of goblet cells. (× 100).

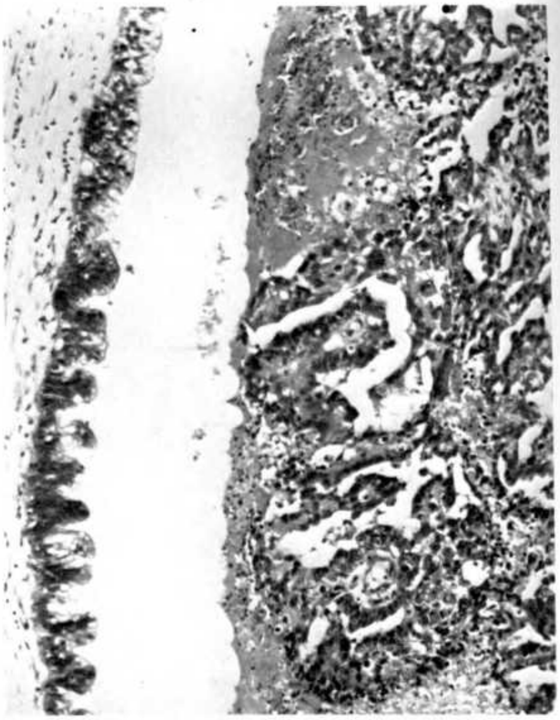


Fig. 5. *Case* 2. Section of mucosal lining of the cystic duplication and moderately differentiated adenocarcinoma within the lumen. The epithelial lining (on the left) shows stratification and cellular atypia. (× 100.)

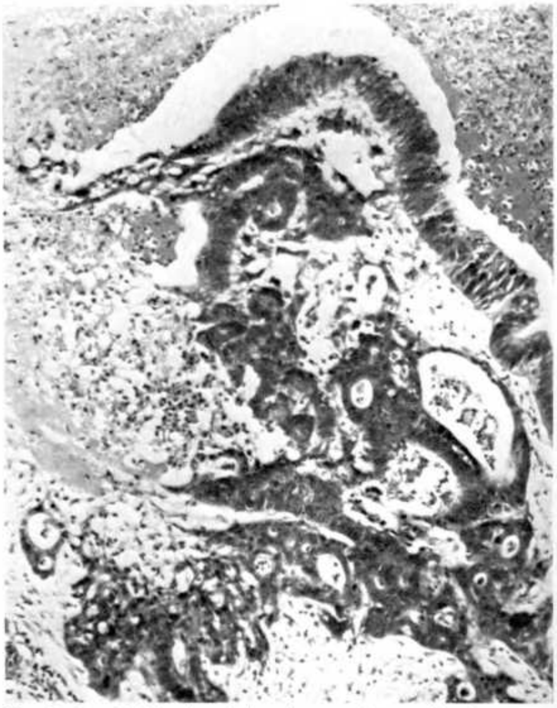


Fig. 6. *Case* 2. Margin of the adenocarcinoma showing infiltration of the cyst wall. Note epithelial atypia present. (× 100).

a marked shift to the left and a slightly raised ESR. Three stools were negative for occult blood, and a chest X-ray, barium enema examination and intravenous pyelogram were all normal.

At laparotomy on 30 October 1972 the hard mass was found to be a chronic abscess in the medial wall of the ascending colon. A limited right hemicolectomy was performed and later histological examination showed that the abscess was due to non-specific perforation of the bowel wall without evidence of tuberculosis, Crohn's disease or neoplasm.

Exploration of the abdomen revealed a sausage-shaped structure, resembling distended small bowel, in the left side of the transverse mesocolon. It was 11 cm long and quite separate from the bowel, although it had a discrete vascular pedicle arising from the root of the superior mesenteric vessels. There was a firm pale nodule 2 cm in diameter in the wall of the tubular structure at its medial end (*Fig.* 1). No enlarged lymph nodes were encountered on mobilizing this apparent duplication, which was excised with its pedicle. The rest of the colon, liver and other viscera were normal.

The patient made an uneventful recovery and has remained well since.

PATHOLOGY: The sausage-shaped structure showed two diverticula on its mesenteric aspect and the whole was filled with brownish mucoid coagulum (*Fig.* 2). Sections confirmed that it was a duplication of the intestine lined by mucus-secreting columnar epithelium and a double-layered smooth muscle coat (*Fig.* 3). The whitish nodule consisted of poorly differentiated adenocarcinoma arising from the mucosal lining of the duplication and there were changes suggestive of carcinoma-in-situ in an extensive field around the frankly neoplastic area (*Fig.* 4). The growth showed penetration through the muscle coat but no evidence of extension outside the wall.

Case 2: Mrs V. S., a 41-year-old postwoman, presented with a 6-week history of pain in the right lower abdomen and backache. The abdominal pain was a constant dull ache, unrelated to eating or other activities, and there were no associated gastro-intestinal symptoms. The only relevant episodes in her medical history were an anterior colporrhaphy 5 months before and an appendicectomy in 1948.

Physical examination revealed a small tender mass in the right iliac fossa, and a subsequent barium enema examination showed this mass to be anteromedial to the ascending colon which was itself normal.

A few days later the patient was admitted urgently with a severe exacerbation of pain in the region of the mass, again with no associated symptoms. On examination she was apyrexial with a normal pulse. There was, however, abdominal tenderness which was maximal over the small mass in the upper right iliac fossa. The mass was 5 cm in diameter, tense and fairly mobile. Pelvic examination was normal. Routine examination of the blood and plain X-rays of the chest and abdomen were normal.

Her pain gradually subsided but the tender mass remained. Laparotomy on 28 October 1968 revealed a rounded cyst adherent to the medial wall of the ascending colon, but with no evidence of inflammation or invasion. There was no other abnormality in the abdomen so the cyst was dissected off the colon and removed without opening the bowel lumen. Full bacteriological examination of the fluid contents of the cyst was negative.

The patient made an uneventful recovery and has remained fit. Two subsequent barium enema examinations showed no abnormality of the colon.

PATHOLOGY: The cyst measured 4 cm in diameter and the wall was up to 2 cm thick with a mainly smooth lining. It contained thick glairy fluid. Sections confirmed the enterogenous nature of the cyst but also revealed an intracystic papillary adenocarcinoma of moderate differentiation. The growth showed invasion of the thin fibrous wall which contained no muscle. The lining of the cyst was varied, with ciliated columnar, cubical and stratified epithelium with atypia adjoining the frankly cancerous epithelium (*Figs.* 5, 6). Calcification beneath the epithelium and in necrotic tumour suggested that the cyst had been present for many years.

Discussion

The literature on the subject of duplications of the alimentary tract is made confusing by the variety of names given to these anomalies by different authors. These include 'reduplication', 'enteric cysts', 'enterogenous cysts', 'giant diverticula', 'ileum duplex', etc. The limitations of some of these terms are obvious and Ladd and Gross (1940) suggested that the term 'duplication' be used for all such anomalies irrespective of their morphology, site or supposed embryological derivation. This would seem to be a satisfactory general term to use, perhaps qualified by other terms where appropriate.

Duplications result from disturbances in embryonic development and various theories have been proposed as to the actual mechanism (Evans and Keith, 1929; Bremer, 1944). There are two main morphological types of duplication—the cystic and the tubular varieties. The classic 'diverticular origin' based on the embryological observations of Lewis and Thyng (1907) might account for the localized cystic type, but some other mechanism must be responsible for the formation of long tubular duplications. Bremer (1944) suggested that they arose from the abnormal persistence of coalescent chains of vacuoles seen in the solid stage of the primitive entodermal tube at about 6 weeks of intra-uterine life. This theory explains the origin of tubular duplications retaining their connection with the bowel lumen at one or both ends, or in the middle, and particularly those which are blind at both ends and entirely separate from the 'parent' tube (with a shared or separate mesentery). *Case* 1 above is an example of the last-named type in which continued secretion had produced a cystic form with two secondary diverticula.

Where vertebral abnormalities coexist with duplications, particularly those involving the foregut, different processes are probably at fault, e.g. the 'split notochord syndrome' and resulting posterior enteric remnants described by Bentley and Smith (1960). Similarly, major duplications of the large bowel associated with doubling of the bladder and genitalia, spina bifida and other major caudal abnormalities must be determined at the blastocyst stage (Ravitch, 1953). Thus, several different embryological maldevelopments may be responsible for different types of duplication.

Occasionally two or more duplications are found in a single patient (Forshall, 1961), and associated anomalies, most commonly malrotation or atresia, are present in a large proportion of cases—31 per cent of those reported by Gross et al. (1952). It has been suggested by Mellish and Koop (1961) that environmental factors such as trauma and hypoxia are likely to be responsible for both the duplications and any associated anomalies.

In tubular duplications the greater part of the wall contains a full complement of normal layers, but in areas of fusion with the bowel the outer layers are shared. The cystic duplication attached to the bowel wall, as in *Case* 2, often lacks a muscular coat as this layer of the 'parent' tube has either been penetrated by

Table 1: DETAILS OF REPORTED CASES OF MALIGNANT CHANGE IN DUPLICATIONS OF THE ALIMENTARY TRACT

* Presentation	Site and type of duplication	Epithelial lining	Neoplasm	Procedure	Course
Gluteal pain, mass per rectum (38; F)*	Presacral; cystic	Mucus-secreting columnar	Adeno.	Excision	Died at 8 mth[1]
Weakness and malaise, anaemia (64; F)	Stomach; cystic	Columnar epithelium, gastric glands	Adeno. (well diff.), node involved	Subtotal gastrectomy	Well at 1 yr[2]
Abdominal pain, weight loss, tender mass (54; M)	Ileum; tubular	Gastric mucosa, epithelial atypia	Adeno. (poorly diff.), nodes, colon and peritoneum involved	Resection	Died at 3 mth[3]
Back pain, mass per rectum (37; F)	Presacral; cystic	Mucus-secreting columnar	Adeno. (moderately well diff.)	Excision	Recurred at 9 mth[4]
Back and abdominal pain, mass (44; F)	Colon; tubular	Columnar and sq. with epithelial atypia	Sq. car. (well diff.), duodenum involved	Right hemicolectomy with duodenal cuff	Died at 6 years of carcinoma of breast. No recurrence[5]
Abdominal pain, tender mass (61 F)	Caecum; tubular	Colonic mucosa, villous adenoma	Adeno. (multifocal well diff.)	Right hemicolectomy	Well[6]
Incidental finding† (57; F)	Mesocolon; tubular	Mucus-secreting columnar, carcinoma-in-situ	Adeno. (poorly diff.)	Excision	Well at 18 mth[7]
Abdominal pain, tender mass‡ (41; F)	Ileocaecal; cystic	Ciliated columnar, cubical, epithelial atypia	Adeno. (moderately well diff.)	Excision	Well at 6 yr[7]

Adeno., adenocarcinoma; diff., differentiated; sq. car., squamous carcinoma.
* (Age; sex). † *Case* 1. ‡ *Case* 2.
Author: [1] Ballantyne (1932). [2] Mayo et al. (1955). [3] Micolonghi and Meissner (1958). [4] Crowley and Page (1960). [5] Larizadeh and Powell (1965). [6] Tamoney and Testa (1967). [7] Orr and Edwards (1975).

the diverticulum which produces the cyst or been thinned out by enlargement of the cyst.

The mucosal lining of duplications is very variable in type; it may be identical with the neighbouring bowel mucosa, particularly where a communication exists, or it may imitate any other segment of the alimentary or respiratory tract (Nolan and Lee, 1953). Heterotopic gastric mucosa is commonly found, especially at the dilated blind end of a tubular duplication, and it has even been reported in duplications of the rectum (Gross et al., 1952). Several different types of mucosa may be found within a single anomalous structure, whether cystic or tubular.

Duplications tend to produce symptoms early in life. Forshall (1961) described how cysts in the inner layers of the bowel wall produce obstruction by intussusception, whereas those outside the main muscle tube may cause obstruction of the gut lumen. The commonest complications in her tubular group were perforated peptic ulcer and volvulus. Ladd and Gross (1940) reported many cases of haemorrhage, mucosal ulceration or sloughing on an ischaemic basis due to vessel distortion. Major duplications of the large bowel such as 'double-barrelled colon' generally present in early life as a result of obstruction of one or both channels or faecal fistula (Ravitch, 1953). Prompt surgical intervention in cases of abdominal duplications without associated abnormalities gives a good prognosis.

The incidence of duplications in adult life is unknown as such cases do not lend themselves to collected series. Nolan and Lee (1953) found only 19 cases in the literature and the presentations were similar to those of paediatric cases and included intestinal obstruction and haemorrhage, inferior vena caval compression and incidental findings on chest X-ray. Neoplastic change has not often been described and Willis (1967) mentioned only 2 cases—those reported by Crowley and Page (1960) and by Larizadeh and Powell (1965). Lockwood (1882) described a case of tubular duplication of the descending colon terminating in a mass of malignant disease obstructing the sigmoid colon, but there was no histological confirmation and the site of origin of the tumour could well have been in the sigmoid colon rather than in the duplication.

Ballantyne (1932) reported a case of adenocarcinoma in a presacral enterogenous cyst. He reviewed 4 other cases of adenocarcinoma arising in presacral cysts apparently satisfying the criteria of 'post anal intestine' but one occurred in an infant and one other was not fully documented. He pointed out the possibility that such lesions may be complex congenital tumours with a portion only representing the gut, but there was nothing to suggest teratoma in his case. There have been 2 reports of neoplastic change in duplications lined by gastric mucosa, one concerning an intramural cyst of the stomach itself (Mayo et al., 1955) and the other a tubular duplication of the ileum (Micologhi and Meissner, 1958). More recently, Tamoney and Testa (1967) reported a case of adenocarcinoma arising in a villous adenoma in a short tubular duplication of the caecum.

We have been unable to find any reports of malignant change in duplication cysts in the posterior mediastinum although over 100 such cysts have been recorded (Anderson, 1971). Malignant neoplasms may arise in Meckelian diverticula, but these congenital abnormalities are much more common and they differ both embryologically and morphologically from duplications of the bowel (Moore and Parsons, 1953).

The main feature of 8 well-documented cases of neoplastic change in duplications of the bowel are summarized in *Table I*. Five of the duplications were apparently large bowel derivatives, lined, at least in part, by mucus-secreting columnar epithelium. All but one of the anomalies either communicated with the bowel or were attached to it, the one exception being found within the transverse mesocolon (the present *Case* 1). The predominance of females (7 : 1) is interesting in view of the higher incidence of carcinoma of the colon in the male. All the patients were under 65 years of age and 4 were under 45 years. The presentations have been varied but most patients had pain and only one presented with an unrelated condition. In 6 cases there was a palpable mass which was generally tender.

The histological features of the tumours are unremarkable in that only one was not typical adenocarcinoma of colonic or gastric type; the single squamous carcinoma arose in an area of squamous epithelium probably representing oesophageal mucosa. However, it is noteworthy that the mucosal lining of the duplication in 5 cases showed changes ranging from epithelial atypia to carcinoma-in-situ at the edge of the frank carcinoma. This evidence of epithelial instability suggests a tendency to undergo malignant transformation. In this connection it is clear that ingested but unabsorbed agents or degradation products of normal bowel contents acting as carcinogens cannot be responsible for the lesions in the *sequestrated*, as opposed to communicating, duplications reported here, whatever their place in carcinogenesis in the colon proper (Willis, 1967; Burkitt, 1970). It is, however, possible that some agent normally excreted by the large bowel mucosa may accumulate within a duplication and exert a carcinogenic effect as a result of absolute or relative stasis. The absence of any reports of cases of malignant change in total duplication of the colon treated by a distal re-entry procedure in childhood is consistent with such a mechanism. Whatever the cause it seems clear that duplications of the large bowel are prone to undergo malignant change.

Many of the tumours had reached an advanced stage by the time of presentation and, judging by the mortality in this admittedly small group, the prognosis would seem to be poor. Two patients surviving at 1 year had shown evidence of local spread of the disease at operation. It is not surprising that neoplasms in duplications entirely separate from the alimentary tract should reveal themselves at a later stage than those in the bowel lumen because typical symptoms such as alteration in bowel habit and bleeding per rectum will not occur. The tumour in *Case* 1 had already penetrated the muscle coat when it came to light incidentally, otherwise its presentation might have been long delayed. Barium studies may be non-contributory unless local distortion is produced by the duplication or invading carcinoma. In the absence of a palpable mass, therefore, it may prove very difficult to reach a diagnosis, and even if a tumour is suspected it is rarely that the correct diagnosis is made preoperatively. Duplications communicating with the bowel lumen or within the wall may show up on barium examination and in one case the meoplasm itself has been demonstrated (Tamoney and Testa, 1967).

Once a duplication has been diagnosed it should clearly be removed, even if it is not causing symptoms, because of the risk of future malignant change. In adult cases the possibility of a neoplasm being present should determine a generous clearance of the surrounding tissues and vascular pedicle although this will entail resection of the related loop of bowel.

It is possible that neoplastic change is not such an uncommon complication in the small proportion of duplications that persist into adult life. Indeed the evidence available from the few cases reported, in the incidence both of frank carcinoma and epithelial atypia, suggests that duplication of the large bowel should be classed as a premalignant condition.

Acknowledgements

We are grateful to Mr P. Stringer and Dr J. I. Pugh of St Alban's City Hospital for permission to publish the second case report. We are also indebted to Dr A. G. Stansfield of St Bartholomew's Hospital for reporting on the histology and to Professor R. A. Willis for his interest and advice.

References

ANDERSON W. A. D. (1971) *Pathology*, 6th ed. St Louis, Mosby, p. 989.

BALLANTYNE E. N. (1932) Sacrococcygeal tumours. *Arch. Pathol.* **14**, 1–9.

BENTLEY J. F. R. and SMITH J. R. (1960) Developmental posterior enteric remnants and spinal malformations. *Arch. Dis. Child.* **35**, 76–86.

BREMER J. L. (1944) Diverticula and duplications of the intestinal tract. *Arch. Pathol.* **38**, 132–140.

BURKITT D. P. (1970) Relationship as a clue to causation. *Lancet* **2**, 1237–1240.

CROWLEY L. V. and PAGE H. G. (1960) Adenocarcinoma arising in presacral enterogenous cyst. *Arch. Pathol.* **69**, 64–66.

EVANS A. and KEITH A. (1929) Developmental enterogenous cysts and diverticula. *Br. J. Surg.* **17**, 34–83.

FORSHALL I. (1961) Duplications of the intestinal tract. *Postgrad. Med. J.* **37**, 570–589.

GROSS R. E., HOLCOMB G. W. and FARBER S., (1952) Duplications of the alimentary tract. *Pediatrics* **9**, 449–468.

LADD W. E. and GROSS R. E. (1940) Surgical treatment of duplications of the alimentary tract. Enterogenous cysts. Enteric cysts or ileum duplex. *Surg. Gynecol. Obstet.* **70**, 295–307.

LARIZADEH R. and POWELL D. F. B. (1965) Neoplastic change in a duplicated colon. *Br. J. Surg.* **52**, 666–668.

LEWIS F. T. and THYNG F. W. (1907) The regular occurrence of intestinal diverticula in embryos of the pig, rabbit and man. *Am. J. Anat.* **7**, 505–519.

LOCKWOOD C. B. (1882) On abnormalities of the caecum and colon with reference to development. *Br. Med. J.* **2**, 574–577.

LO PRESTI J. M., KAUFMAN P. and HAWFIELD H. H. (1949) Duplications of the alimentary tract. *Clin. Proc. Child. Hosp.* (*Wash.*) **6**, 357–361.

MAYO H. W., MCKEE E. E. and ANDERSON R. M. (1955) Carcinoma arising in reduplication of stomach (gastrogenous cyst): a case report. *Ann. Surg.* **141**, 550–555.

MELLISH R. W. P. and KOOP C. E. (1961) Clinical manifestations of duplications of the bowel. *Pediatrics* **27**, 397–407.

MICOLONGHI T. and MEISSNER G. F. (1958) Gastric type carcinoma arising in duplication of the small intestine. *Ann. Surg.* **147**, 124–127.

MOORE R. M. and PARSONS W. H. (1953) Carcinoma of Meckel's diverticulum. *Arch. Surg.* **67**, 939–942.

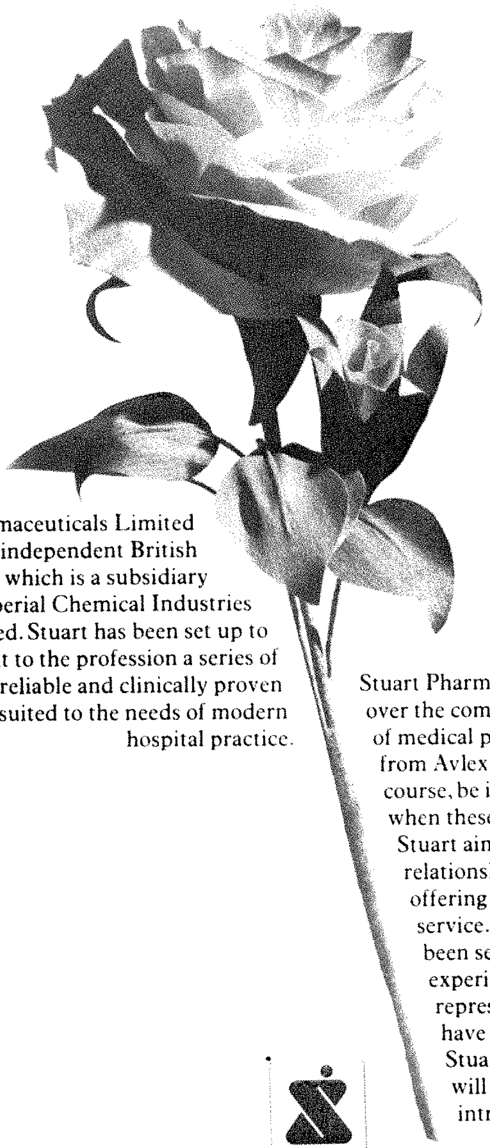
NOLAN J. J. and LEE J. G. (1953) Duplications of the alimentary tract in adults with a report of 3 cases. *Ann. Surg.* **137**, 342–348.

RAVITCH M. M. (1953) Hind gut duplication—doubling of colon and genital urinary tracts. *Ann. Surg.* **137**, 588–601.

TAMONEY H. J. and TESTA R. E. (1967) Carcinoma arising in a duplicated colon—case report. *Cancer* **20**, 478–481.

WILLIS R. A. (1967) *Pathology of Tumours*, 4th ed. London, Butterworths, pp. 419–423.

Stuart blossoms



Stuart Pharmaceuticals Limited is a new, independent British Company which is a subsidiary Company of Imperial Chemical Industries Limited. Stuart has been set up to present to the profession a series of reliable and clinically proven products suited to the needs of modern hospital practice.

Stuart Pharmaceuticals will, over the coming year, market a variety of medical products currently available from Avlex Limited. You will, of course, be informed separately as and when these changes occur.

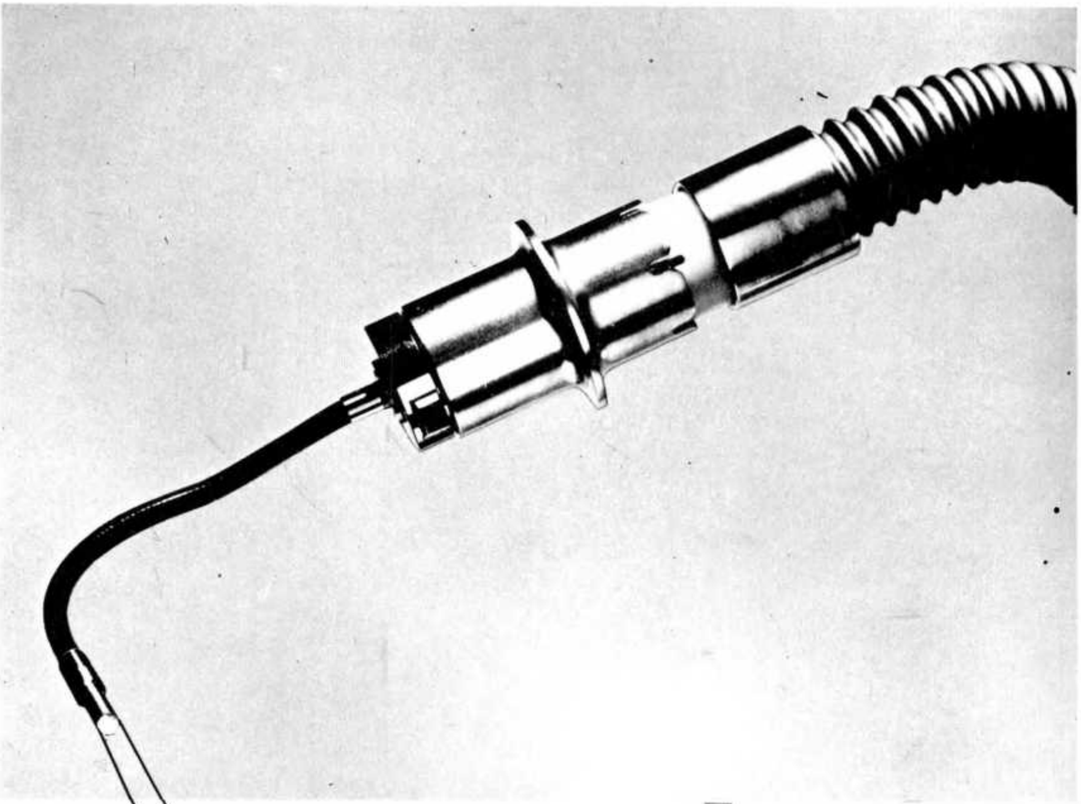
Stuart aims to develop a good working relationship with the profession by offering an efficient and courteous service. To ensure this all staff have been selected for their previous experience and before any Stuart representative calls on you he will have received extensive training in the Stuart range of products. Now if you will kindly turn over the page we will introduce the first of our products.

STUART

new

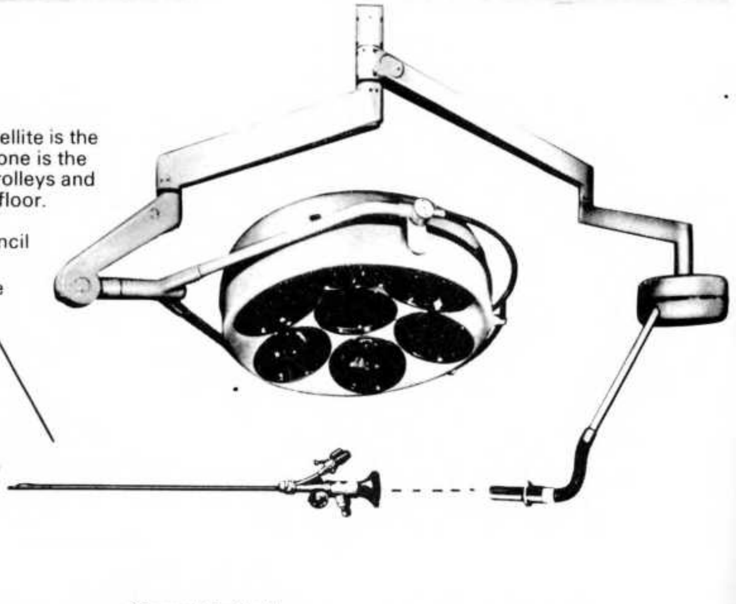
SIEREX

FLEXIBLE PENCIL LIGHT



The Boston lamp with its GFO Satellite is the ideal endoscopic light source. Gone is the need for a separate source, for trolleys and mains cables trailing across the floor.

Illustrated above is a flexible pencil light, ideal for Neuro and ENT surgery, shown connected to the GFO Satellite.



Most glass-fibre endoscopic instruments can be connected in this way.

Sierex

Sierex Limited

15/18 Clipstone Street, London, W1P 8AE, 01-580 2464
Branches in *Aberdeen, Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester and Reading.*
Agents in *Belfast, Newcastle and Newport.*

DISPRAY I
Trade Mark
Quick Prep
Chlorhexidine gluconate 0.5% w/v in 70% I.M.S.
Stuart Pharmaceuticals Limited Cheadle, Cheshire.
DISPRAY 2
Hard Surface Disinfectant
Chlorhexidine gluconate 0.02% w/v in 70% I.M.S.
Stuart Pharmaceuticals Ltd Cheadle, Cheshire.

DISPRAY I
TRADE MARK
Quick Prep
Chlorhexidine Gluconate 0.5% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for skin disinfection

'Dispray' 1 Quick Prep.
(formerly known as Hibispray 1)
is an ideal preparation for skin and
hand disinfection in the busy
hospital environment.
At the touch of a button it gives
fast, easy and economical
skin disinfection prior to surgery,
injection or venepuncture.
When colour delineation
is required eg. pre-operatively,
'Dispray' 3 is available
with a red dye.

The 'Dispray' range
combines effectiveness with
convenience and economy.

Instant Availability.
No solutions to prepare.

Easy to use.
No swabs or bottles required.

Quick and Effective.
Rapid bactericidal action.

Efficient Application.
No wasted solutions.

Contents cannot
be contaminated.
No rejected solutions.

Long Lasting.
Contents of one can treat 100 sq. ft.

'Dispray' 1, 2, 3.
The Pick of the Bunch
for Disinfection.

DISPRAY 2
TRADE MARK
Hard Surface
Disinfectant
Chlorhexidine Gluconate 0.02% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for hard surface disinfection

'Dispray' 2 Hard Surface
Disinfectant (formerly known as
Hibispray 2) provides rapid
disinfection of all hard surfaces
throughout the hospital.
Trolleys, cabinets, cupboards,
working surfaces – even footwear,
are rapidly, effectively
and efficiently disinfected.

Further
information
is available
from:

STUART

Stuart
Pharmaceuticals
Limited,
Carr House,
Carrs Road,
Cheadle,
Cheshire SK8 2EG.

"I Bring Peace"-73

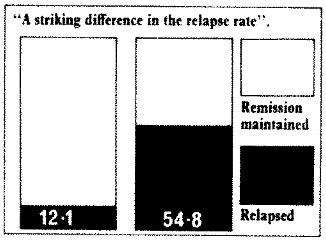
"It is concluded that maintenance treatment of ulcerative colitis with sulphasalazine (salazopyrin) should be continued indefinitely unless contraindicated by side effects".[1]

The results of the above controlled trial carried out at the Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford are all the more welcome as earlier trials of cortisone[2] and prednisone[3] at standard dosages have shown them to be ineffective in reducing the number of recurrences of ulcerative colitis.

"Fortunately, Sulphasalazine tablets, 0.5 grams 4 times a day will prevent relapses in the majority of patients with colitis, and only a few patients cannot tolerate this relatively small dose, which can be continued indefinitely since we do not know when, if ever, it can be safely stopped".[4]

Salazopyrin (sulphasalazine) is available as the plain 0.5g. tablet, 0.5g. EN-tab and as an 0.5g. suppository. Literature and detailed information on Salazopyrin are available on request.

Salazopyrin is a registered trade mark.



"The patients who received dummy tablets had more than four times the relapse rate of those receiving sulphasalazine".[1] (Salazopyrin).

Both groups of patients had been satisfactorily maintained for 1-5 years on Salazopyrin prior to the study, in which they took Salazopyrin or placebo for 6 months.

References
1. Gut (1973) *14* 923-926
2. Brit. med. J. (1959) *1* 387-394
3. Lancet (1965) *i* 188-189
4. General Practitioner (1972) April 7 p11

Salazopyrin

– to be continued indefinitely

Further information on request from:–
Pharmacia (Great Britain) Ltd.
Paramount House,
75 Uxbridge Road,
London W5 5SS.
Telephone: 01-579 0102/7

Pharmacia

Br. J. Surg. Vol. 62 (1975) 275–279

A controlled trial of parenteral prophylactic gentamicin therapy in biliary surgery

M. R. B. KEIGHLEY, R. M. BADDELEY, D. W. BURDON, J. A. C. EDWARDS,
A. H. QUORAISHI, G. D. OATES, G. T. WATTS AND J. ALEXANDER-WILLIAMS*

SUMMARY

This trial has investigated the value of gentamicin therapy in patients requiring biliary surgery. One hundred consecutive patients were randomly allocated to receive either gentamicin or no antibiotic. Postoperative infection was assessed by an independent observer. Cultures and gentamicin assays were performed on bile and blood sampled during and after operation. The minimum inhibitory concentrations of gentamicin were measured with isolated bacteria.

In 80 per cent of patients biliary organisms were inhibited by 2 μg/ml of gentamicin. Twice this concentration was found in the serum at operation in 88 per cent, but in the bile in only 18 per cent. Nevertheless, gentamicin lowered the incidence of bacteria in the bile from 42 to 25 per cent. There was a reduction in wound sepsis from 21 to 6 per cent ($P < 0{\cdot}05$). Bacteriaemia was demonstrated in only 1 patient receiving gentamicin compared with 5 controls and 1 death occurred from endotoxaemia in the control group.

These data suggest that gentamicin will reduce the morbidity of biliary surgery, particularly in patients in whom the bile is infected at operation.

HIGH colony counts of pathogenic bacteria are found in the bile in a third of patients operated upon for biliary disease (Edlund et al., 1958). The proportion of patients with infected bile is higher in the elderly, in patients with stones in the common bile duct and where emergency operation is considered necessary (Keighley and Graham, 1973). There is a close correlation between the type and presence of bacteria in the bile and the development of postoperative wound sepsis (Robson et al., 1970); also between infected bile and septicaemia (Flemma et al., 1967).

Wound infection is particularly common following biliary surgery (Maxwell et al., 1969). In a prospective study by the Public Health Laboratory Service (Report, 1960) the wound sepsis rate after elective cholecystectomy (20·6 per cent) was similar to that of patients requiring emergency laparotomy for peritonitis. Wound infections complicating gastrointestinal surgery are usually caused by the introduction of endogenous enterobacteria into the incision during operation (Davidson et al., 1971).

Septicaemia is a serious hazard in patients with cholangitis requiring surgical treatment. It is also a complication of diagnostic X-ray procedures involving the injection of contrast material directly into the biliary system (Koch and Gardner, 1969; Williams and Dawson, 1969; Keighley et al., 1974), the main danger being endotoxaemia, which may be complicated by renal failure and which is often fatal (Murdoch et al., 1968). There is a close anatomical relationship between the biliary canaliculi and the liver sinusoids in patients with obstructive jaundice (Edlund and Hanzon, 1953); particles of comparable size to Gram-negative bacteria have been shown to enter the bloodstream from the bile by this route (Huang et al., 1969).

Prophylactic antibiotic therapy will reduce the incidence of postoperative infections, particularly in wounds which become potentially contaminated at operation (Evans and Pollock, 1973). As a result of animal experiments it has been suggested that if antibiotics are to be effective they should be present in the tissues at the time of primary bacterial inoculation (Burke, 1961). In patients requiring biliary surgery the choice of antibiotic will depend upon the sensitivity of the bacteria to various agents and their excretion in the bile. It has been shown, however, that most antibiotics which are commonly found in high concentrations in the bile are inadequately excreted in the presence of obstruction (Schoenfield, 1971). Because most micro-organisms found in the bile are extremely sensitive to gentamicin (Maddocks et al., 1973) and because of the overwhelming importance of avoiding bloodstream infection, gentamicin was chosen for this study.

Materials and methods

One hundred consecutive patients were randomly allocated to a treated group or a control group. Patients receiving gentamicin were given two preoperative 80-mg doses; at 6 a.m. and half-an-hour before leaving the ward for the operating theatre. Although there were occasional delays between the time of the last preoperative dose and operation the interval was never more than 2 hours. This dosage of gentamicin was continued by 8-hourly injections for 5 days after operation.

Exclusion clauses removed from the study any patients where additional surgical procedures (other than appendicectomy or proximal gastric vagotomy) were performed, all cases with malignant obstructive jaundice requiring operation and 1 patient with a previous history of allergy to gentamicin.

The type of abdominal incision, use of subhepatic drains and method of closing a choledochotomy incision were left to the discretion of each surgeon. Drains were used only through a separate wound.

---

* The General Hospital, Birmingham.

Table I: CLINICAL PRESENTATION AND OPERATIVE FINDINGS

	Gentamicin	Controls
Age:		
Less than 50 yr	21	20
50–60 yr	14	6
60–70 yr	7	10
Greater than 70 yr	7	12
Jaundice:		
Never	38	30
Past history only	6	14
Current	5	4
Timing of operation:		
Elective	44	45
Emergency	5	3
Operation:		
Cholecystectomy	35	33
With exploration of the common bile duct	14	15
Drain	28	28
No drain	21	20
Site of stones:		
None	1	3
Confined to the gallbladder	37	34
Common bile duct calculi	11	11

At operation samples of bile were aspirated from the gallbladder for culture and viable counts, and when organisms were isolated their sensitivity and the minimum inhibitory concentration of gentamicin were also measured. When operative cholangiography was performed (93 cases) bile was also collected from the common bile duct, where possible before the injection of contrast. Samples of bile and venous blood were collected at operation and stored at 4 °C for batch gentamicin assay.

Wound infection was assessed on alternate days by an independent observer and was recorded only when pus which contained viable organisms was present in the abdominal incision. This was graded into three categories: stitch abscess, superficial sepsis and deep collections of pus. Infection at the drainage site was classified only if bacteria could be cultured from swabs which were collected on the third and fifth days after operation. Blood cultures were taken immediately after the patient returned to the ward, on the third and seventh postoperative days, after T tube cholangiography and in any patient with an unexplained pyrexia after operation. Serum which was taken 1 hour before and 2 hours after injection on the third postoperative day was stored at 4 °C for gentamicin assay at a later date.

Antibiotics were given to the controls or changed in the treated group only when there was bacteriological evidence of severe postoperative infection where specific antibiotic therapy was considered to be essential.

To avoid dangers of dose-dependent nephrotoxicity and damage to the eighth cranial nerve, all patients receiving gentamicin had daily blood urea estimations performed. There were 3 patients in whom the blood urea rose to above 60 mg/100 ml. Gentamicin assays were then performed during treatment and 1 hour before and 1 hour after injection on every other day. The dose of gentamicin was reduced if the peak and trough concentrations were greater than 12 and 8 µg/ml respectively.

Clinical and bacteriological information was recorded on pre-coded work sheets and stored on punch cards. The data have been analysed using a card-sorting machine.

Detailed microbiological investigations

Fresh samples of bile and infected material were cultured under aerobic and anaerobic conditions on blood agar, MacConkey's agar, neomycin-impregnated agar plates and Selenite broth for up to 72 hours. Bacteria were identified by their cultural properties, colonial appearance, motility and biochemical reactions. Organisms were stored on agar slopes or cooked meat broth. Viable counts were measured using tenfold dilutions of 0·1 ml of bile in agar incubated overnight before counting.

The antibiotic sensitivities of bacteria were judged by the zone of inhibition to standard antibiotic-impregnated discs. The minimum inhibitory concentration (MIC) of gentamicin was measured by adding serial dilutions of antibiotic to agar plates which were inoculated with bacteria isolated from the bile and incubated overnight. The concentration of gentamicin which inhibited the growth completely or up to three colonies was taken as the MIC.

Gentamicin assay was performed by the plate diffusion method using *Bacillus subtilis* as the test organism. Wells cut in the agar were filled with serum, bile or standard dilutions at random. Standard gentamicin solutions were prepared by diluting a stock concentration in normal saline, serum, bile or pH buffer. Because there was no appreciable difference in the inhibition zone of the different diluents normal saline was used for making subsequent standards. For each batch of assays a standard curve was made by plotting the gentamicin concentration on a log scale against the diameter of the inhibition zone. The concentration of gentamicin in bile and serum was calculated by measuring the diameter of the clear inhibition zone which was read off from the standard curve. Each estimation was performed in duplicate.

Results

One hundred consecutive patients undergoing biliary surgery were admitted to the trial. There were 3 patients who were withdrawn after completion of the trial. One patient in the treated group had not been given gentamicin before operation, and there were 2 controls who received antibiotics in the immediate postoperative period without bacteriological evidence of an infective complication. Of the remaining 97 cases, 49 received gentamicin and there were 48 controls.

Although the age of the patients differed in the two groups, their clinical presentation, the site of stones and the type of surgical procedures were similar (*Table I*).

There was a reduction in the incidence of bacteria in the bile at operation from 42 per cent in the controls to 25 per cent in the treated group (*Table II*). Despite this there was no obvious difference in the type of organisms in the bile in each group (*Table III*). With the exception of one bile culture, containing a scanty growth of diphtheroids which was considered to be a contaminant, the remainder were all associated with high colony counts of pathogenic bacteria. The only counts which were less than 10^4 organisms per ml were found in 3 patients where samples had been obtained after operative cholangiography.

There was a significant reduction in the wound sepsis rate from 21 per cent in the controls to 6 per cent in the treated group ($P<0\cdot05$) (*Table IV*). Severe wound infection occurred only in the controls. Organisms were isolated from drain site swabs in 14 of the controls, compared with only 3 cases receiving treatment ($P<0\cdot05$). Blood cultures were positive in only 1 patient receiving gentamicin. This occurred, in the absence of clinical infection, 72 hours after cholecystectomy. In contrast, there were 5 patients with clinical signs of bacteriaemia and with positive blood cultures in the early postoperative period in the control group. One of these patients developed endotoxaemia accompanied by renal failure which was responsible for the only operative death in the study.

The incidence of wound sepsis and bacteriaemia was compared in relation to the presence or absence of bacteria in the bile (*Table V*). When the bile was sterile there was a similar incidence of wound sepsis in both the treated and the control groups. However, in patients with infected bile there was a significant reduction in the wound sepsis rate from 40 per cent in the controls to 8 per cent in patients receiving gentamicin ($P<0\cdot05$).

The concentration of gentamicin required to inhibit the growth of organisms isolated in the bile collected at operation or during T tube drainage is shown in *Table VI*. With the exception of bacteroides, *Clostridium welchii* and certain faecal streptococci, all of the remaining organisms were inhibited by 2 µg/ml of gentamicin.

The concentrations of gentamicin in the bile and the serum are shown in *Table VII*. Gentamicin concentrations which were greater than twice the MIC for 85 per cent of biliary micro-organisms (4 µg/ml) were considered to be 'adequate'. Using this figure, 'adequate' concentrations of gentamicin were present in the gallbladder and common bile duct in 18 and 3 per cent of patients respectively. In contrast, satisfactory antibiotic concentrations were found in the serum at operation in 88 per cent of cases. There was also a striking resemblance between the serum gentamicin assays at operation and samples taken 2 hours after injection on the third postoperative day. This suggests that the time interval between the last preoperative injection and removal of the gallbladder rarely exceeded 2 hours. To measure the normal levels of gentamicin in the bile, repeated samples were obtained in 7 patients with T tubes on continual drainage 3 days after operation (*Table VIII*). Only one of these patients had an 'adequate' concentration of gentamicin in the bile 1 hour after injection.

Table II: BACTERIA IN THE BILE AT OPERATION

	Gentamicin	Controls
No bacteria	37	28
Bacteria isolated	12 (25%)	20 (42%)

Table III: TYPE OF ORGANISMS IN THE BILE AT OPERATION

Organism	Gentamicin	Controls	Total
Escherichia coli	4	14	18
Klebsiella aerogenes	2	5	7
Streptococcus faecalis	3	5	8
Streptococcus viridans	2		2
Proteus sp.		2	2
Staphylococcus aureus	—	2	2
Anaerobic streptococci	1		1
Diphtheroids	1		1
Clostridium welchii		3	3
Bacteroides sp.		1	1
Enterobacter cloacae	2		2
Enterobacter aerogenes	1		1

Table IV: POSTOPERATIVE INFECTION

	Gentamicin		Controls	
Wound sepsis		3 (6%)		10 (21%)*
Stitch abscess	0		2	
Superficial sepsis	3		5	
Deep	0		3	
Drain site infection		3 (6%)		14 (29%)*
Infected bile	1		3	
Purulent exudate	2		11	
Bacteriaemia		1		5 (NS)

* P<0·05. NS, Not significant.

Table V: INCIDENCE OF WOUND SEPSIS AND SEPTICAEMIA IN RELATION TO THE PRESENCE OR ABSENCE OF BACTERIA IN THE BILE

	Gentamicin		Controls	
	No.	%	No.	%
Sterile bile	37		28	
Wound sepsis	2	5	2	7 (NS)
Bacteriaemia	0		1	4 (NS)
Infected bile†	12		20	
Wound sepsis	1	8	8	40*
Bacteriaemia	1	8	4	20 (NS)

* $P<0\cdot05$. NS, Not significant.

† With one exception organisms isolated in the wound and bloodstream were identical to those in the bile.

Discussion

This study has shown that prophylactic gentamicin given before and for 5 days after operation is associated with a significant reduction in the wound sepsis rate after biliary surgery when the bile is infected. Also infection around the drain site and bacteriaemia were reduced after operation in the treated group.

Bacteria in the bile have previously been shown to be particularly sensitive to gentamicin (Keighley and Graham, 1973; Maddocks et al., 1973). We chose to study gentamicin in the belief that postoperative morbidity is closely related to the presence of Enterobacteriaceae in the bile at operation. As far as we are

Table VI: MINIMUM INHIBITORY CONCENTRATION OF GENTAMICIN FOR ALL ORGANISMS ISOLATED IN THE BILE

MIC (μg/ml)	*E. coli*	*Kl. aerogenes*	*Str. viridans*	*Str. faecalis*	*Ps. aeruginosa*	*Ent. aerogenes*	*Ac. anitratus*	*Ent. cloacae*	*Staphylococcus* sp.	*Bacteroides* sp.	*Proteus* sp.	*Cl. welchii*	Diphtheroids	Total
0·06													1	1
0·125	1								2					3
0·25	2	2												4
0·5	11	3		2	1	1	1	2	2		1			24
1·0	8	1	2	2	2		2	1			1			19
2·0	1		1	2				1			1	1	1	8
4·0				2								1		3
8·0												2		2
>8·0				2						3				5

Table VII: GENTAMICIN ASSAY

Gentamicin level (μg/ml)	At operation			Postoperative	
				Serum	
	Gallbladder	Common bile duct	Serum	1 hr before injection	2 hr after injection
'Adequate' (>2 × MIC for 85% of organisms)					
>16	2	1	4	2	4
8–16	1	0	16	1	16
4–8	5	0	22	12	25
'Inadequate' (<2 × MIC for 85% of organisms)					
2–4	15	9	5	23	2
<2	22	20	1	10	1
Total	45	30	48	48	48

Table VIII: GENTAMICIN LEVELS IN BILE IN 7 PATIENTS WITH T TUBE DRAINAGE

Gentamicin level (μg/ml)	1 hr before injection	After injection		
		1 hr	2 hr	4 hr
>16	0	0	0	0
8–16	0	0	0	0
4–8	0	1	0	0
2–4	0	2	1	0
<2	7	4	6	7

aware, the value of gentamicin in patients requiring biliary surgery has not been previously studied.

Because we chose to use a fixed dose of gentamicin it could be argued that some of the patients received insufficient antibiotic for adequate prophylaxis. Nevertheless with only one exception concentrations measured 3 days after operation were within the acceptable range 2 hours after injection.

Gentamicin has been used cautiously in routine prophylaxis because of the dangers of renal impairment and ototoxicity in patients on prolonged therapy or with renal failure. Precautions were taken to prevent this by monitoring serum levels of gentamicin during treatment in patients with an elevated blood urea. Although routine tests of vestibular and auditory function were not performed during this trial there was no clinical evidence of ototoxicity. There were 4 patients with serum gentamicin levels which were greater than 16 μg/ml in the presence of normal renal function. The reason for these extremely high levels has been unexplained.

The aminoglycosides are known to be poorly excreted in the bile. Although there is little information concerning the biliary excretion of gentamicin (Smithivas, 1971) we did not expect to find high concentrations, particularly if there was any degree of biliary obstruction. It has been assumed that high concentrations of antibiotic should be present in the bile if chemotherapy is to be effective in patients undergoing biliary surgery (Twiss et al., 1956; Acocella et al., 1968; Chetlin, 1973). However, the results of this trial have shown that serum antibiotic concentrations were more important than biliary gentamicin levels in reducing postoperative sepsis. The results of serum gentamicin assay demonstrated concentrations of gentamicin which were usually at least two or three times greater than the MIC of all organisms in the bile apart from bacteroides, *Clostridium welchii* and certain faecal streptococci. The relative merits of serum and biliary antibiotic levels as a means of preventing postoperative infection are currently being studied.

Routine prophylactic antibiotic therapy has often been condemned in the majority of patients undergoing elective surgical treatment on the basis that chemotherapy is rarely beneficial and may encourage.

the emergence of resistant bacteria (Altemeier et al., 1956). However, the results of this study have shown that prophylactic gentamicin will reduce the incidence of bacteriaemia and wound infection, particularly when bacteria are present in the bile at the time of operation. For this reason it would seem more logical to advise antibiotic cover only in patients whose biliary tract is liable to be colonized by pathogenic bacteria at operation. We already know that patients with calculous obstructive jaundice are particularly prone to bacteriaemia and that high colony counts of Gram-negative bacteria can be isolated in 90 per cent of these cases (Scott and Khan, 1967). There is also a high incidence of bacteria in the bile in the elderly requiring elective operation and in patients with acute cholecystitis (Watson, 1969). Prophylactic gentamicin therapy should therefore be advised in these patients. We are currently studying the value of an immediate Gram stain on centrifuged bile to detect the presence and type of infecting organism in order that a policy of prophylactic antibiotic therapy given at operation can be adopted. This would be a valuable way of avoiding unnecessary prophylaxis which sooner or later is likely to be associated with resistant organisms and super-infection (Garrod, 1972).

References

ACOCELLA A., MATTIUSSI R. B., NICHOLAS F. B., PALLANZA R. and TENCONI L. (1968) Biliary excretion of antibiotics in man. *Gut* **9**, 536–545.

ALTEMEIER W. A., CULBERTSON W. R. and VELTO M. (1956) Prophylactic antibiotic therapy. *Arch. Surg.* **71**, 2–6.

BURKE J. F. (1961) The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery* **50**, 161–168.

CHETLIN S. H. (1973) Pre-operative antibiotics in biliary surgery. *Arch. Surg.* **107**, 319–323.

DAVIDSON A. I. G., SMITH G. and SMYLIE H. G. (1971) A bacteriological study of the immediate environment of a surgical wound. *Br. J. Surg.* **58**, 326–333.

EDLUND Y. A. and HANZON V. (1953) Demonstration of the close relationship between bile capillaries and sinusoidal wall. *Acta Anat.* **17**, 105–109.

EDLUND Y. A., MOLLSTEDT B. O. and OUCHTERLONY O. (1958) Bacteriological investigation of the biliary system and liver in biliary tract disease correlated to clinical data and microstructure of the gallbladder and liver. *Acta Chir. Scand.* **116**, 461–476.

EVANS C. and POLLOCK A. V. (1973) The reduction of surgical wound infection by prophylactic parenteral cephaloridine. *Br. J. Surg.* **60**, 434–437.

FLEMMA R. J., FLINT L. M., OSTERHOUT S. and SHINGLETON W. W. (1967) Bacteriological studies of biliary tract infection. *Ann. Surg.* **166**, 563–572.

GARROD L. P. (1972) Causes of failure in antibiotic treatment. *Br. Med. J.* **4**, 473–476.

HUANG T., BASS J. A. and WILLIAMS R. D. (1969) The significance of biliary pressure in cholangitis. *Arch. Surg.* **98**, 629–632.

KEIGHLEY M. R. B. and GRAHAM N. G. (1973) Infective cholecystitis. *J.R. Coll. Surg. Edinb.* **18**, 213–220.

KEIGHLEY M. R. B., LISTER D. M., JACOBS S. I. and GILES G. R. (1974) Hazards of surgical treatment due to micro-organisms in the bile. *Surgery* **75**, 578–583.

KOCH R. L. and GARDNER J. L. (1969) Bile blood fistula: a complication of percutaneous transhepatic cholangiography. *Radiology* **93**, 67–68.

MADDOCKS A. C., HILSON G. R. F. and TAYLOR R. (1973) The bacteriology of the obstructed biliary tree. *Ann. R. Coll. Surg. Engl.* **52**, 316–319.

MAXWELL J. G., FORD C. R., PETERSON D. E. and RICHARDS R. C. (1969) Abdominal wound infections and plastic drape protectors. *Am. J. Surg.* **118**, 844–848.

MURDOCH J. MCC., SPIERS C. F. and PULLEN H. (1968) The bacteraemic shock syndrome. *Br. J. Hosp. Med.*, **1**, 346–353.

REPORT (1960) Public Health Laboratory Service Report. *Lancet* **2**, 659–663.

ROBSON M. C., BOGART J. C. and HEGGERS J. P. (1970) An endogenous source for wound infection based on quantitative bacteriology of the biliary tract. *Surgery* **63**, 471–476.

SCHOENFIELD L. J. (1971) Biliary excretion of antibiotics. *New Engl. J. Med.* **184**, 1213–1214.

SCOTT A. J. and KHAN G. A. (1967) Origin of bacteria in bile duct bile. *Lancet* **2**, 790–792.

SMITHIVAS T. (1971) Gentamicin and ampicillin in human-bile. *J. Infect. Dis.* **124**, 100–113.

TWISS J. R., GILLETTE L., BERGER W. V., ARONSON A. R. and SEIGEL L. (1956) The role of antibiotics in infections of the biliary tract: studies of sensitivity and biliary tract excretion. *Ann. Surg.* **144**, 1008–1012.

WATSON J. F. (1969) The role of bacterial infection in acute cholecystitis: a prospective clinical study. *Milit. Med.* **134**, 416–426.

WILLIAMS R. and DAWSON J. T. (1969) The management of ascending cholangitis. *Proc. R. Soc. Med.* **62**, 243–244.

Br. J. Surg. Vol. 62 (1975) 280–283

Operative biopsy of the pancreas

PHYLLIS GEORGE, COLIN BROWN AND JAMES GILCHRIST*

SUMMARY

A review has been undertaken of the 47 patients who have had open pancreatic biopsy performed at the Royal Free Hospital between 1967 and 1972. It is concluded that not only is the procedure safe when using the technique described but also it is a valuable and accurate diagnostic procedure.

TAKING biopsies from the pancreas has usually been regarded as a hazardous procedure. For this reason a retrospective study has been undertaken of patients who had open pancreatic biopsies performed during the course of a laparotomy. All the patients were operated on at the Royal Free Hospital between 1967 and 1972 and all were under the care of one surgeon (P. G.). Patients who had transduodenal pancreatic biopsies were excluded from the series. The purpose of this study was to determine whether or not the procedure was safe and whether worthwhile information could be obtained.

Indications

The commonest indication for biopsy (*Cases* 1–35) was to obtain histological confirmation of a suspected carcinoma in patients who had no extrapancreatic spread of the disease but in whom radical surgery had not been undertaken because of the degree of local extension or because of the patient's age or general condition. (Patients who had metastases had the metastatic deposit biopsied and thus were not included in the series.)

Pancreatic biopsies were also taken from patients (*Cases* 36–47) in whom the nature of the pancreatic pathology was in doubt, and also from patients who had preoperative investigations suggesting pancreatic disease but who had a macroscopically normal pancreas at operation. Some illustrative case histories from the latter group are given below.

Case reports

Case 36: A 53-year-old male had a 2-month history of diabetes mellitus and had had one episode of superficial thrombophlebitis in his leg. A barium meal examination was normal but a pancreatic scan suggested a small filling defect in the head of the pancreas.

At laparotomy the gland felt normal. Biopsies were taken from the head, body and tail, all of which showed normal pancreatic tissue. The patient is alive and well 4½ years later.

Case 37: A 48-year-old woman had undergone laparotomy for obstructive jaundice at another hospital when a large mass, thought to be a carcinoma, was found in the head of the pancreas, but no biopsy was taken. A cholecystectomy and choledochojejunostomy were performed and the patient's family was told that she had only a few months to live.

Six months later, when the patient was apparently well, she was referred for a decision as to whether the lesion might be resectable. At operation the pancreas was macroscopically normal, biopsies being taken from the head and body of the gland and also from the para-aortic and mesenteric lymph nodes. All were histologically normal. It was thought that the 'tumour' seen at the original operation probably was a haematoma formed following coeliac axis arteriography. The patient is alive and well 20 months after her second laparotomy.

Case 39: A 43-year-old man complained of anorexia and weight loss. A barium meal and follow through examination showed a widened duodenal loop and an abnormal mucosal pattern at the duodenojejunal flexure.

At laparotomy the pancreas was uniformly thickened, the small and large bowel being macroscopically normal. Three pancreatic biopsies were normal but a full thickness bowel biopsy taken from the duodenojejunal flexure showed lymphoma.

Cases 41, 42 and 43: These patients were explored for obstructive jaundice and found to have biliary calculi and considerable localized thickening of the pancreatic head. There was doubt, macroscopically, as to whether these lesions were areas of chronic pancreatitis or carcinoma, but all the biopsies taken showed chronic pancreatitis. The patients are alive and well 50, 30 and 20 months after operation respectively.

Case 44: A 71-year-old woman was admitted as an emergency with upper abdominal pain and vomiting. On examination she was pyrexial, with tenderness in the epigastrium and right hypochondrium. A plain abdominal X-ray showed gallstones, and her serum amylase was normal. She was diagnosed as having acute cholecystitis, but as her condition did not improve with conservative treatment a laparotomy was performed.

At operation the head of the pancreas was enlarged and oedematous; the gallbladder was full of stones but not inflamed. The common bile duct was not dilated. A cholecystectomy and choledochojejunostomy were performed for a presumed pancreatic carcinoma. However, pancreatic biopsy showed the changes of acute pancreatitis, and the patient is alive and well 4½ years later.

Case 45: A 52-year-old woman with primary biliary cirrhosis was operated on for repeated haematemeses; a large duodenal ulcer was found associated with marked induration in the pancreas, thought to be either carcinoma or reaction to the adjacent ulcer. A biopsy of the affected area of the pancreas showed no evidence of malignancy. The patient died 18 months later of hepatic failure; autopsy confirmed the diagnosis of primary biliary cirrhosis with a normal pancreas.

Case 47: A 51-year-old male underwent laparotomy for recurrent ulceration following a Polya gastrectomy. At operation there was a firm nodule in the body of the pancreas which was thought possibly to be an alpha-cell tumour. This was excised. Histology showed multinucleated giant cells containing birefringent material surrounded by normal pancreatic tissue.

Technique

The anterior surface of the gland is exposed by opening the lesser sac. Inspection and palpation of the head and posterior aspect of the gland can adequately be achieved after incising the posterior parietal peritoneum around the outer edge of the first and second parts of the duodenum; the duodenum and head of the pancreas can then be turned to the left (Kocher's manœuvre).

---

* Departments of Surgery and Histopathology, Royal Free Hospital, London.

The biopsy itself is taken from the most superficial and firmest part of the lesion using a tenotomy knife—a small pyramid (0·3 × 0·3 × 0·3 cm) of tissue is removed. The exposed raw area is covered with either a piece of Oxycel (surgical) or omentum, lightly held in place by two chromic catgut sutures (in the manner of patching a perforated ulcer). A drain is routinely placed in the area and shortened over the subsequent 5 days.

Laboratory diagnosis

All biopsies were treated in the routine manner in the laboratory and stained with haematoxylin and eosin, multiple levels being cut in cases where the diagnosis was not at once apparent. One frozen section was performed and the histology subsequently confirmed on paraffin wax sectioning. On only two occasions was it deemed necessary to request special stains to exclude a rare diagnosis.

Results

Between 1967 and 1972 there were 47 patients who had wedge biopsies of the pancreas. Their ages ranged from 19 to 84 years. The patients are considered in two groups: first those who at operation were thought to have a primary carcinoma of the pancreas (group 1), and secondly those who at operation were thought to have either pancreatic pathology other than carcinoma or a normal pancreas (group 2).

Group 1

There were 35 patients in this group; the average age was 55 years (range 23–84 years).

In 31 patients (88 per cent) the biopsy confirmed the clinical diagnosis. There were 4 patients in whom the biopsy proved inadequate for diagnosis. Two of these patients have since died and autopsy verified the operative diagnosis. The other 2 patients are alive, 12 and 21 months respectively after operation.

All the patients in group 1 had a palliative biliary bypass (usually a choledochojejunostomy with an entero-enterostomy) in addition to the pancreatic

Table I: COMPLICATIONS IN GROUP 1

Case no.	Age	Sex	Complication	Outcome
3	50	F	Biliary fistula	Closed spontaneously
7	64	M	Burst abdomen	Resutured. No further complication
10	64	F	Bronchopneumonia	Recovered
12	70	M	Coronary thrombosis	Died 10 hours post-operatively
18	70	F	Hepatorenal failure	Died 10 days post-operatively
19	81	M	Burst abdomen	Resutured. No further complication
21	62	F	Bronchopneumonia	Died 16 days post-operatively
26	48	F	Gram-negative septicaemia	Died 8 days post-operatively
29	64	F	Infected wound	Delayed wound healing

All these patients had a biliary bypass performed for an inoperable pancreatic carcinoma.

Table II: DETAILS OF PATIENTS IN GROUP 2

Case No.	Age	Sex	Operative diagnosis	Procedure other than pancreatic biopsy	Pancreatic biopsy report	Follow-up
36	53	M	Normal pancreas	None	Normal pancreas	Alive and well after 4½ years
37	48	F	Normal pancreas	Lymph node biopsies	Normal pancreas	Alive and well after 20 months
38	19	M	Solitary pancreatic cyst	Marsupialization of hydatid cyst	Normal pancreas	Alive and well after 9 months
39	43	M	? Chronic pancreatitis	Multiple tissue biopsies	Normal pancreas	Alive and well after 1 year
40	54	M	Chronic pancreatitis	Drainage of cyst	Chronic pancreatitis	Died after 1 month of respiratory failure. No post-mortem
41	57	F	Chronic pancreatitis	Cholecystectomy and exploration of common bile duct	Chronic pancreatitis	Alive and well after 50 months
42	64	F	Chronic pancreatitis	Cholecystectomy and exploration of common bile duct	Chronic pancreatitis	Alive and well after 30 months
43	60	F	Chronic pancreatitis	Cholecystectomy and exploration of common bile duct	Chronic pancreatitis	Alive and well at 20 months
44	71	F	? Acute pancreatitis ? Carcinoma of pancreas	Cholecystectomy and bypass	Acute pancreatitis	Alive and well at 4½ years
45	52	F	? Chronic pancreatitis	Vagotomy and gastro-enterostomy	Normal pancreas	Died after 9 months in liver failure secondary to primary biliary cirrhosis. Post-mortem showed primary biliary cirrhosis and normal pancreas
46	64	M	1. Portal hypertension 2. Mass in body and head of pancreas	Undersewing of gastric varices	Cystadenoma	Died after 2 days of haemorrhage from varices. Post-mortem showed cystadenoma of pancreas
47	51	M	? Alpha cell tumour of pancreas	Vagotomy	Foreign body reaction	Alive and well after 5½ years

biopsy. Nine patients (*Table I*) developed postoperative complications, none of which, however, could be attributed to the biopsy.

Group 2

There were 12 patients in this group (6 males and 6 females). These patients required a variety of operative procedures in addition to having pancreatic biopsy. The operative diagnosis, biopsy report and subsequent follow-up are all summarized in *Table II.*

There were 2 postoperative deaths; one (*Case* 40) died of respiratory failure, and the other (*Case* 46) continued to bleed from his gastric varices. An autopsy in the latter case confirmed that the biopsy was correct.

One other patient (*Case* 45) died 9 months later from hepatic failure. An autopsy confirmed that the pancreas was normal. The other 9 patients are alive and well.

Discussion

With the exception of acute pancreatitis, the nature of pancreatic disease is not always readily diagnosable by the usual investigations. In particular it may be difficult, even at operation, to distinguish between carcinoma and chronic pancreatitis. Pancreatic biopsy seems an obvious step but has usually been regarded as both dangerous and uninformative (Cattell and Warren, 1951).

There are two particular aspects of pancreatic biopsy to be considered: namely whether it is safe, and *only if it is*, is it worthwhile?

Safety

It is generally taught that the pancreas should not be biopsied directly because of the risks of haemorrhage, fistulas, abscess formation, pancreatitis or subphrenic abscess (Moyer et al., 1965; Schultz and Sanders, 1963; Maingot, 1969). For these reasons various authors have advocated that pancreatic biopsies, if they are going to be taken at all, should be taken either transduodenally using a Vim Silverman needle or by excision through the duodenal wall, thus deliberately creating a fistula between the gland and the duodenum (Willbanks and Razzuk, 1971). If the pancreatic lesion involves the lower end of the common bile duct adequate tissue for histological diagnosis may be obtained by curettings taken from within the bile duct (Hall and Krementz, 1968).

The reported complications of pancreatic biopsy have to be evaluated very critically as frequently other surgical procedures are performed at the same time. Forsgren et al. (1968) had only 1 complication in a series of 50 cases that could be attributed to biopsy. Williams et al. (1960) presented a series of 43 cases who underwent a wedge biopsy of the pancreas in addition to having a biliary bypass. These patients were compared with similar number in which only a bypass was performed, and there was no significant difference in either operative morbidity or mortality.

In our series none of the postoperative complications could be attributed to the biopsy. It is felt that the procedure is safe using the technique described, provided that the biopsy can be kept as superficial as possible and care is taken not to biopsy in the region of the main pancreatic duct. If the duct is inadvertently opened then it should be intubated, the tube being brought out to the surface via the stomach, thus producing a pancreaticogastric fistula (Smith, 1972).

Value of biopsy

It is always important to obtain histological confirmation of any pathology for several reasons:

1. The clinical diagnosis may be confirmed or proved incorrect.
2. It may influence subsequent therapy.
3. It may help in giving a more reliable prognosis.
4. It is essential to know the true pathology when comparing different modes of therapy or palliation.

In this series there were 2 patients aged 23 and 24 respectively who had inoperable carcinoma of the pancreas. No matter how 'certain' one may be at operation of the diagnosis, one is still extremely reluctant to make the diagnosis in patients of this age without histological proof. Conversely, *Case* 37 provides an example in which both the patient and her relatives were informed that she had an inoperable carcinoma and had only a few months to live (and she made arrangements for her cremation), when in fact she had a benign lesion.

Any biopsy, and particularly a small one, is subject to two main sources of error, namely: errors of interpretation and errors of sampling. It was possible to review all the histological slides in the series and no errors of interpretation were found. It is the second source of error, namely of sampling, that the critics of pancreatic biopsy emphasize (Bowden, 1954; Schultz and Sanders, 1963).

It is well known that a small pancreatic carcinoma may be surrounded by an extensive area of pancreatitis and this necessarily forms the outermost layer of the tumour, which is the part most readily accessible to the biopsy knife. Hence the carcinoma may not on occasion be biopsied but merely the area of pancreatitis. The incidence of false negatives varies widely in reported series, but figures of 12 per cent or even 54 per cent are quoted (Probstein et al., 1950; Spjut and Ramos, 1957; Cote et al., 1959).

All the patients in our series have been carefully followed up. In group 1 positive biopsies were obtained in 31 out of 35 patients thought to have carcinoma, i.e. in 88 per cent of cases—figures almost identical to those of Williams et al. (1960).

In group 2 only time will show the final accuracy of the biopsies. In the 2 patients who came to autopsy the biopsy report was found to be correct. All the rest of the patients are alive and well, and in particular the 3 patients thought to have chronic pancreatitis have no signs of a carcinoma at 50, 30 and 20 months after operation respectively.

It is concluded that pancreatic biopsy is of value. If carcinoma is found, then there is unequivocal proof of the lesion. If chronic pancreatitis or a normal pancreas is found then there is *contributory* evidence of a non-malignant condition. In the vast majority of cases (91 per cent in this series) worthwhile reliable information will be obtained.

Acknowledgements
We should like to thank Professor Sherlock, who referred the majority of the patients to one of us (P. G.), Professor Ian Bouchier for helpful criticism and Dr P. Scheuer of the Department of Histopathology. We are also grateful to Mrs N. Last and Mrs R. Timings for their secretarial assistance.

References

BOWDEN L. (1954) The fallibility of pancreatic biopsy. *Ann. Surg.* **139**, 403–408.

CATTELL R. B. and WARREN K. W. (1951) Pancreatic surgery. *New Engl. J. Med.* **244**, 975–982.

COTE J., DOCKERTY M. B. and PRIESTLEY J. T. (1959) An evaluation of pancreatic biopsy with the Vim–Silverman needle. *Arch. Surg.* **79**, 588–596.

FORSGREN L., HANSSON K., LUNDH G. and NORDENSTAM H. (1968) Pancreatic biopsy. *Acta Chir. Scand.* **134**, 457–460.

HALL R. C. and KREMENTZ E. T. (1968) Diagnosis and treatment of pancreatic cancer. *Br. J. Hosp. Med.* **1**, 168–178.

MOYER C. A., RHOADS J. E., ALLEN J. G. and HARKINS H. N. (1965) *Surgical Principles and Practice*, 3rd ed., ch. 31. London, Pitman.

MAINGOT R. (1969) *Abdominal Operations*, 5th ed., ch. 36. New York, Appleton-Century-Crofts.

PROBSTEIN J. G., SACHAR L. A. and RINDSKOPF W. (1950) Biopsies of pancreatic masses. *Surgery* **27**, 356–359.

SCHULTZ N. J. and SANDERS R. J. (1963) Evaluation of pancreatic biopsy. *Ann. Surg.* **158**, 1053–1057.

SMITH R. (1972) Operative manual of exocrine pancreatic disease. *Clin. Gastroenterol.* pp. 239–256.

SPJUT H. J. and RAMOS A. J. (1957) An evaluation of biopsy—frozen section of the ampullary region and pancreas. *Ann. Surg.* **146**, 923–930.

WILLBANKS O. L. and RAZZUK M. A. (1971) Improved incisional biopsy technique for lesions of the head of the pancreas: construction of pancreatico-duodenostomy at biopsy site. *Surgery* **69**, 84–86.

WILLIAMS R. D., ELLIOTT D. W. and ZOLLINGER R. M. (1960) Surgery for malignant jaundice. *Arch. Surg.* **80**, 992–997.

Br. J. Surg. Vol. 62 (1975) 284–286

Carcinoma of the large bowel in the Sudan

S. H. ELMASRI AND P. B. BOULOS*

SUMMARY

Large bowel cancer is not common but is showing increased frequency in the northern part of the Sudan. It is relatively uncommon among southerners, which may be due to the socio-economic factors prevailing in the Sudan.

The disease affected our population at a younger age than has been generally reported in the literature, and the lesions in nearly 30 per cent were of the mucoid and undifferentiated types.

The incidence in young adults is difficult to explain in the absence of precancerous lesions, and there is not enough evidence to incriminate parasitic infestation.

The incidence of carcinoma of the large bowel has been of great interest to many workers particularly in African countries, where it has been reported to be relatively lower than in affluent societies.

Wynder and Shigematsu (1967) and Burkitt (1971) believed that this relatively low incidence in African countries could be explained on the basis of diet and the socio-economic background of these countries. If this is true, then it would be reasonable to expect a rising incidence of carcinoma of the large bowel in an African community which is progressively moving up the socio-economic ladder and gradually acquiring the dietary habits of Western society.

Materials and methods

We have reviewed the histopathological reports of all specimens of carcinoma of the large bowel received in the Central Research Laboratory, Khartoum, during the period 1963–72. In this laboratory, specimens from all over the country are examined, and accordingly this analysis reflects the overall pattern of this disease in the Sudan.

The results were analysed with regard to annual incidence, sex and age distribution, site of the lesions and their histological appearances.

Results

There were 272 specimens of large bowel cancer; 203 were in the anorectum and 69 in the colon. The sex distribution was 167 males and 105 females, a ratio of roughly 5 : 3. The same ratio was maintained in patients with anorectal cancer and in those with colonic cancer (*Table I*).

The average age for carcinoma of the colon was 44·5 years and that for cancer of the anorectum was 52·3. Of 203 patients with anorectal cancer, 159 (78 per cent) were below the age of 60, while of 69 patents with colonic cancer, 59 (85 per cent) were below this age. Of the whole series, 43 patients were below the age of 30; 34 (16·5 per cent) with anorectal and 9 (14 per cent) with colonic lesions (*Tables II, III*).

The anatomical and histological distributions are shown in *Tables IV* and *V*.

Table I: SEX DISTRIBUTION IN CANCER OF THE COLON AND ANORECTUM

Sex	Colon	Anorectum	Total
Males	42	125	167
Females	27	78	105
Total	69	203	272

Table II: SEX AND AGE DISTRIBUTION IN ANORECTAL CANCER

	Sex		
Age group	Male	Female	Total
0–9	—	—	—
10–19	3	2	5
20–29	17	12	29
30–39	23	10	33
40–49	22	20	42
50–59	30	20	50
60–69	24	12	36
70–79	4	2	6
80–89	2	—	2
Total	125	78	203

Table III: SEX AND AGE DISTRIBUTION IN CANCER OF THE COLON

	Sex		
Age group	Male	Female	Total
0–9	—	—	—
10–19	1	1	2
20–29	5	2	7
30–39	13	5	18
40–49	11	6	17
50–59	7	8	15
60–69	5	3	8
70–79	—	2	2
80–89	—	—	—
Total	42	27	69

Discussion

Unlike many other published series, we have included as large bowel cancer squamous cell carcinoma of the anal canal. In fact, such cancers form a surprisingly high proportion of our series, comprising about one-quarter of the anorectal cancers and about one-fifth of the entire series of large bowel cancers. In the Sudan, therefore, there is a much higher relative incidence of squamous cell cancer of the anal region than is reported from Western countries, for which there is no obvious explanation.

---

* Department of Surgery, University of Khartoum, Sudan.
Requests for reprints to S. H. ElMasri, Lecturer in Surgery, Department of Surgery, Faculty of Medicine, PO Box 102, Khartoum, Sudan.

Carcinoma of the large bowel has been described in all age groups. The youngest reported was in a premature infant (Ahfeld, 1880). The youngest in this series was in a boy of 14; 16·5 per cent of our patients with anorectal cancer and 14 per cent with colonic cancer were below the age of 30. These percentages are significantly higher than those reported by other workers, which range between 1 and 9·2 per cent (Recio and Bussey, 1965; Sessions et al., 1965; O'Brien 1967; Miller and Liechty, 1967; Rosato et al., 1969; Gallagher and Michael, 1972).

Van Langenberg and Ong (1972) reviewed a total of 582 cases of large bowel cancer collected since 1961 and found 21 cases (3·6 per cent) in young adults. Their ages ranged between 13 and 25 years. While Goligher (1941) noticed that more than half of his patients with rectal cancer were above the age of 60, 78 per cent of our patients with anorectal cancer and 85 per cent with colonic cancer were below this age.

Why this is so is a matter for speculation. It could be due to the fact that the population at risk in the Sudan is of a younger age group than in other series. The fact that a relatively high proportion of young patients has been affected by large bowel cancer in this series might be associated with the relatively high proportion (29 per cent) of undifferentiated and mucoid types of carcinoma.

Goligher (1967) and Morson (1968) reported an incidence of 25–30 per cent of benign polyps in resected specimens for large bowel cancer. However, precancerous lesions of the large bowel are rare in Africa (Burkitt, 1971; Stewart, 1971). In none of our resected specimens was there any evidence of polyposis, ulcerative colitis or coexisting benign polyps. In only one specimen was there a bilharzial granuloma with ova surrounded by squamous cell carcinoma.

Hickey (1959), reviewing a total of 1337 cases of cancer seen in the Sudan during the period 1935–54 (20 years), found 74 histologically confirmed specimens of large bowel cancer. Seven of these were in the colon while 67 occurred in the anorectum. Lynch et al. (1963), in a similar study of 2234 cases of cancer during the period 1954–61 (8 years), reported 62 cases of cancer of the large bowel, giving an incidence of 2·78 per cent. Twenty-three were in the colon and 39 in the anorectum. In the present analysis (1963–72) the incidence of carcinoma of the large bowel was 4·04 per cent out of a total of 6725 cases of cancer. It appears from these figures that during the latter period there has been a significant increase not only in the total number of cancers detected but also in cancer of the large bowel (*Table VI*). It is tempting to relate this relatively higher incidence of large bowel cancer to factors relevant to the socio-economic development witnessed by this country during the period of the present analysis. Amongst the factors described in the literature to predispose to large bowel cancer is a fibre-depleted diet which delays bowel evacuation and therefore exposes the bowel mucosa to carcinogens for prolonged periods (Burkitt, 1971). It is perhaps relevant at this juncture to note that only 2 cases of large bowel cancer in this series were encountered from the Southern Sudan, where the transit time in the large bowel has been found to be shorter than in a group of subjects in the Northern Sudan (Osman, 1973). However, as there are other differences between the population in Southern and Northern Sudan, we do not feel that it is justifiable to conclude that dietary factors alone are responsible for the increasing incidence of large bowel cancer in the Northern Sudan.

It is quite conceivable that other factors related to socio-economic development might explain this increased incidence of large bowel cancer, e.g. increased detection of cancer due to improvement in health services, health education, etc., in which case this relatively high incidence of large bowel cancer would be an apparent rather than a real one.

Table IV: HISTOPATHOLOGICAL ANALYSIS OF 203 CASES OF ANORECTAL CANCER

	No. of cases
Adenocarcinoma	
Differentiated	104
Undifferentiated	22
Mucoid	24
Squamous cell carcinoma (anal canal)	53
Total	203

Table V: ANATOMICAL AND HISTOPATHOLOGICAL ANALYSIS OF 69 CASES OF COLONIC CANCER

	Adenocarcinoma			
Site	Diff.	Undiff.	Mucoid	Total
Caecum	8	2	6	16
Ascending colon	4	3	1	8
Hepatic flexure	3	3	0	6
Transverse colon	3	3	0	6
Splenic flexure	2	0	0	2
Descending colon	2	2	2	6
Sigmoid colon	14	7	4	25
Total	36	20	13	69

Diff., Differentiated. Undiff., Undifferentiated.

Table VI: INCIDENCE OF ALL CANCERS AND OF LARGE BOWEL CANCER IN THE SUDAN

	Author	No. of cases of cancer	Cancer of the large bowel
1935–54 (20 years)	Hickey (1959)	1337	73
1954–61 (8 years)	Lynch et al. (1963)	2234	62
1963–72 (10 years)	Present study	6725	272

Acknowledgements

We are grateful to Dr Sayed Dawoud, Director of the Central Research Laboratory, for making the records of the Sudan Cancer Registry available for this analysis.

We also wish to thank Mr Mohamed Ahmed Hassan, Senior Lecturer in the Department of Surgery, for his help in the preparation of this paper.

References

AHFELD F. (1880) Zur Casusistik der Congenitalen Neoplasmen. *Arch. Gynaekol.* **16**, 135.

BURKITT D. P. (1971) Epidemiology of cancer of the colon and rectum. *Cancer* **28**, 3–13.

GALLAGHER E. G. and MICHAEL G. Z. (1972) Rectal carcinoma in patients in the second and third decades of life. *Am. J. Surg.* **124**, 655–659.

GOLIGHER J. C. (1941) The operability of carcinoma of the rectum. *Br. Med. J.* **2**, 393–397.

GOLIGHER J. C. (1967) *Surgery of the Anus, Rectum and Colon*, 2nd ed. London, Baillière, Tindall & Cassel, p. 418.

HICKEY B. B. (1959) Malignant epithelial tumours in Sudanese. *Ann. R. Coll. Surg. Engl.* **24**, 303–322.

LYNCH J. B., HASSAN A. M. and OMER A. (1963) Cancer in the Sudan. *Sudan Med. J.* **2**, 29–37.

MILLER F. E. and LIECHTY R. D. (1967) Adenocarcinoma of the colon and rectum in persons under thirty years of age. *Am. J. Surg.* **113**, 507–510.

MORSON B. C. (1968) Precancerous and early malignant lesions of the large bowel. *Br. J. Surg.* **55**, 725–731.

O'BRIEN S. E. (1967) Carcinoma of the colon in child-hood and adolescence. *Can. Med. Assoc. J.* **96**, 1217–1219.

OSMAN A. A. (1973) Personal communication.

RECIO P. and BUSSEY H. J. R. (1965) The pathology and prognosis of carcinoma of rectum in the young *Proc. R. Soc. Med.* **58**, 789–790.

ROSATO F. E., FRAZIER T. G., COMPELAND E. M. and MILLER I. D. (1969) Carcinoma of the colon in young people. *Surg. Gynecol. Obstet.* **129**, 29–32

SESSIONS R. T., RIDDELL D. H., KAPLAN H. J. and FORSTE J. H. (1965) Carcinoma of the colon in the firs two decades of life. *Ann. Surg.* **162**, 279–284.

STEWART H. L. (1971) Geographical pathology o cancer of the colon and rectum. *Cancer* **28**, 25–28

VAN LANGENBERG A. and ONG G. B. (1972) Carcinoma o large bowel in the young. *Br. Med. J.* **3**, 374–376

WYNDER E. L. and SHIGEMATSU T. (1967) Environmenta factors of cancer of colon and rectum. *Cancer* **20** 1520–1561.

Wellcome

References
1. *Postgrad med J.* (1971) **47**, Supplement (September) 7.
2. *Brit med J.* (1972), **2**, 673.
3. *Clin Trials J.* (1972), **9/3**, 9.

SEPTRIN contains trimethoprim and sulphamethoxazole.
Full prescribing information is available on request.
Wellcome Medical Division,
The Wellcome Foundation Ltd.,
Berkhamsted, Herts.

Feels right for Septrin

b.d. in urinary infections

When clinical examination reveals urinary infection in children, experience increasingly indicates the need for the prompt, vigorous action of SEPTRIN Paediatric Suspension.

Rated top oral treatment in a British survey of 23,491 urinary pathogen sensitivities,[1] SEPTRIN has been judged superior to ampicillin,[2,3] and is now well established as a first-line treatment for urinary infections.

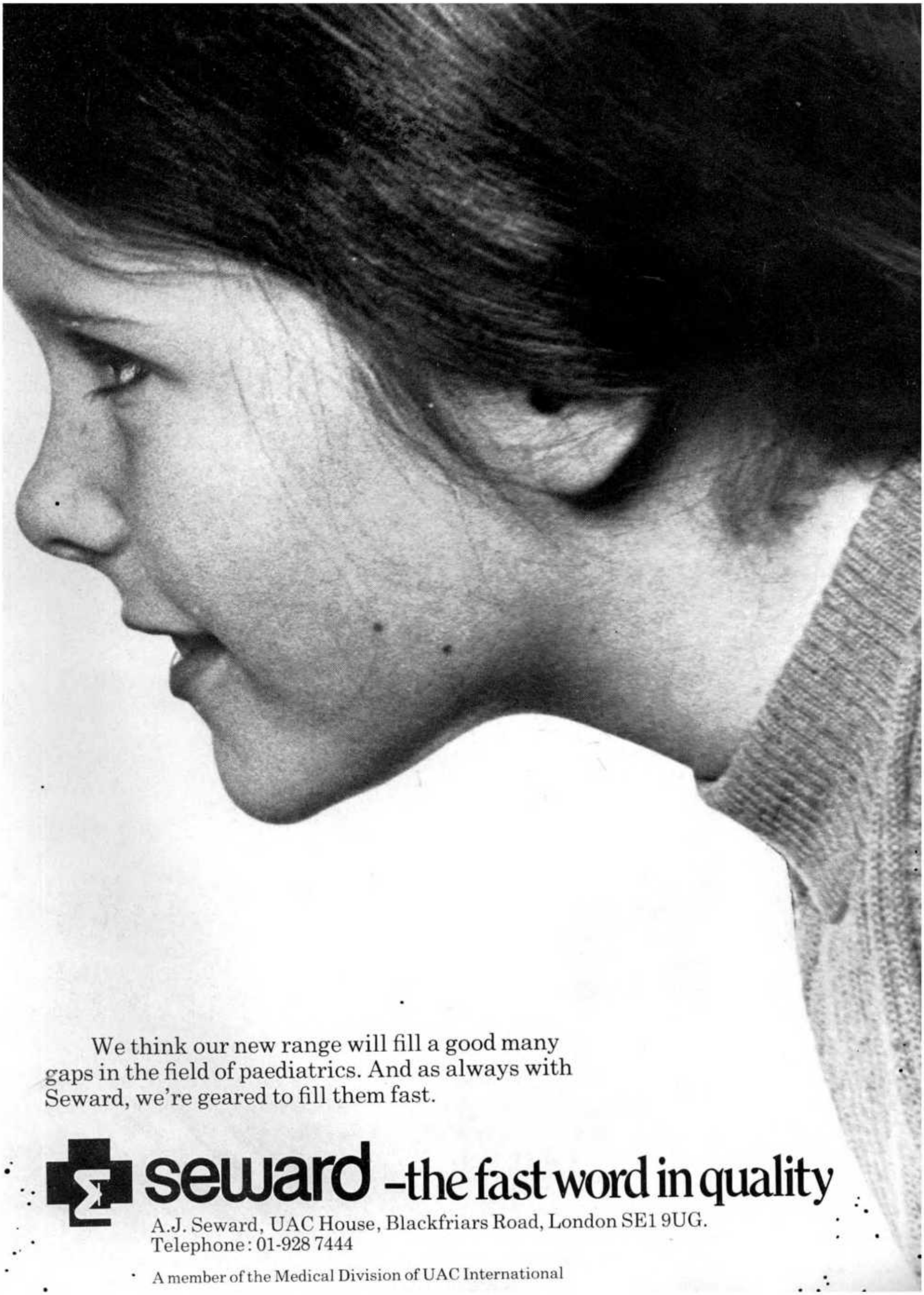
SEPTRIN TRADE MARK
Paediatric Suspension

Now paediatrics gets the Seward treatment.

At Seward, we believe that instruments for paediatric surgery are every bit as important as adult instruments.

That's why we spent a long time developing and perfecting our own paediatric range – and we're grateful for the co-operation of so many children's hospitals, paediatric departments and consultants.

Now the range is complete – 580 fine quality stainless steel instruments. Including many which have never before been modified for paediatric use. And some entirely new instruments developed in the Seward workshop.



We think our new range will fill a good many gaps in the field of paediatrics. And as always with Seward, we're geared to fill them fast.

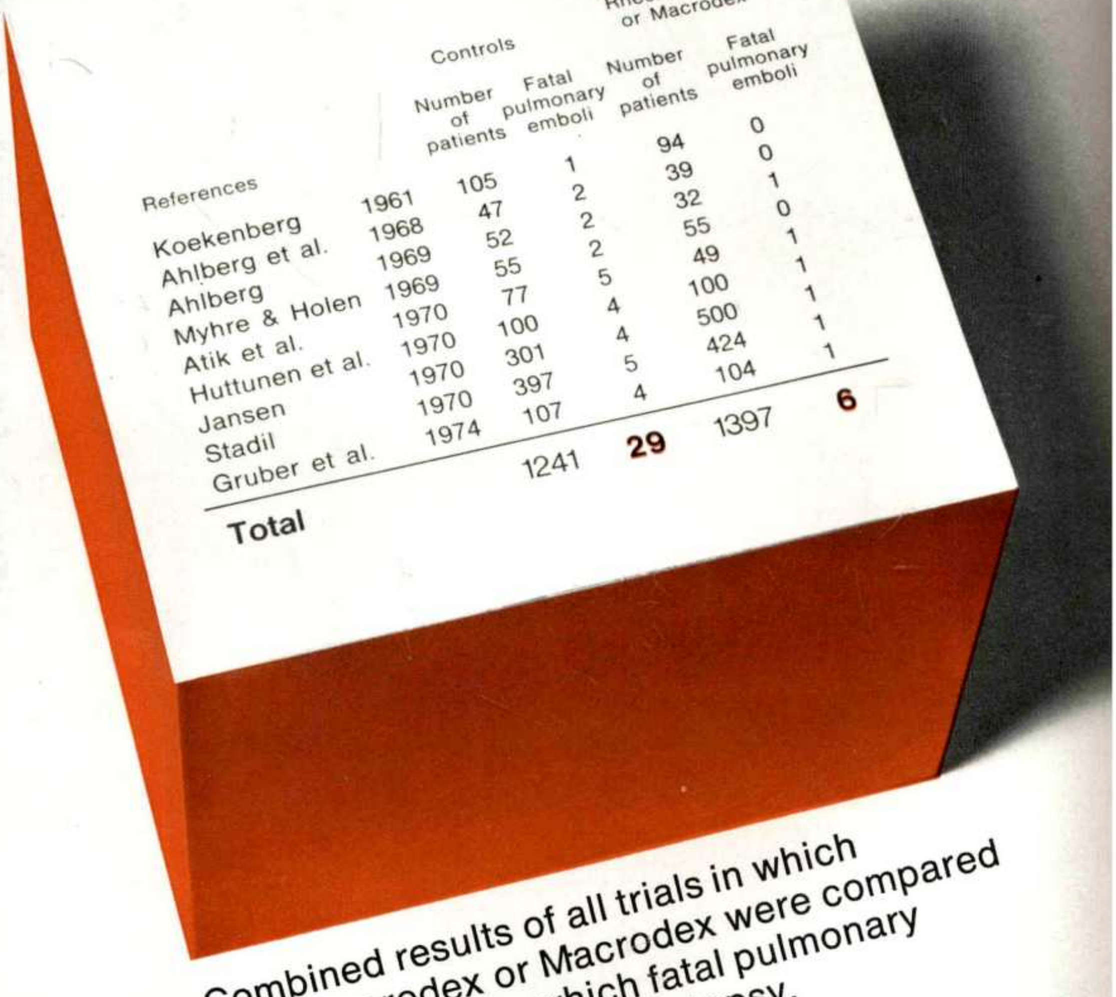
seward –the fast word in quality

A.J. Seward, UAC House, Blackfriars Road, London SE1 9UG.
Telephone: 01-928 7444

A member of the Medical Division of UAC International

Compelling evidence mounts up:

Rheomacrodex and Macrodex reduce mortality from post-operative pulmonary embolism!



References		Controls		Rheomacrodex or Macrodex	
		Number of patients	Fatal pulmonary emboli	Number of patients	Fatal pulmonary emboli
Koekenberg	1961	105	1	94	0
Ahlberg et al.	1968	47	2	39	0
Ahlberg	1969	52	2	32	1
Myhre & Holen	1969	55	2	55	0
Atik et al.	1970	77	5	49	1
Huttunen et al.	1970	100	4	100	1
Jansen	1970	301	4	500	1
Stadil	1970	397	5	424	1
Gruber et al.	1974	107	4	104	1
Total		1241	**29**	1397	**6**

Combined results of all trials in which Rheomacrodex or Macrodex were compared to controls and in which fatal pulmonary emboli were verified by autopsy.

Pharmacia

Pharmacia (Great Britain) Limited,
Paramount House,
75 Uxbridge Road,
London W5 5SS

Rheomacrodex and Macrodex comply with the dextran 40 and 70 BP 1973 monographs respectively.

Br. J. Surg. Vol. 62 (1975) 287–291

A controlled clinical trial of three different methods of perineal wound management following excision of the rectum

T. T. IRVIN AND J. C. GOLIGHER

SUMMARY

Three methods of perineal wound closure were studied in a randomized prospective clinical trial in 106 patients undergoing excision of the rectum for inflammatory or malignant disease. In method 1 the perineal wound was managed by open drainage. In both methods 2 and 3 the perineal wound was closed by primary suture, suprapubic suction drains being left down to the presacral space, but in method 2 the pelvic peritoneal floor was reconstituted, whilst in method 3 it was left unsutured. Topical and systemic antibiotics were administered to all patients submitted to primary closure of the perineal wound but not routinely to those whose perineal wound was left open.

The overall operative mortality was 8·5 per cent but no deaths could be definitely attributed to perineal wound complications. The incidence of primary wound healing after methods 2 and 3 was 45·2 and 42·9 per cent respectively. Operative contamination of the perineal wound had an adverse effect on perineal wound healing. The incidence of persistent wound sinuses and unhealed wounds at 3 and 6 months after primary wound closure was rather less than that encountered after open drainage.

It was concluded that primary closure of the perineal wound is the treatment of choice following excision of the rectum, except in cases in which contamination of the perineal wound has occurred during operation or the final state of haemostasis in the pelvis with diathermy and suture at the conclusion of the dissection was deemed to be unsatisfactory.

One of the major sources of discomfort and concern to patients who have undergone excision of the rectum is the perineal wound. Traditionally this wound is left partly open and packed (Miles, 1908, 1926), or only partially closed around a wound drain (Gabriel, 1963). In either event the wound must be regularly irrigated and partly repacked during the postoperative period, and several uncomfortable weeks or months may elapse before healing is complete.

Recently, it has been suggested that primary suture of the perineal wound may obviate much of the inconvenience of the traditionally managed perineal wound after rectal excision and may be followed by primary healing in a significant proportion of cases (Oates and Alexander-Williams, 1970; Hultén et al., 1971; Altemeier et al., 1974; Broader et al., 1974). The failures recorded after primary suture have been due to abscess or haematoma formation in the presacral space below the pelvic peritoneum, and Ruckley et al. (1970) attempted to overcome this problem by incorporating a pedicled omental graft in the dead space below the pelvic peritoneal floor. Another simple method which various surgeons (e.g. Haxton, 1970) have used in the past in an effort to overcome the problem of the presacral dead space is to avoid suturing the pelvic peritoneum altogether, thus permitting the small intestine to occupy the pelvic cavity.

However, we have been unable to discover any strictly objective published data on the relative merits of these different modifications of technique and have thus been prompted to institute a prospective randomized properly controlled clinical trial of two different methods of primary closure of the perineal wound against the traditional method of open drainage.

Materials and methods

Methods of perineal wound management on trial

The three methods being tried were:

Method 1. *Open drainage*: The pelvic peritoneum was sutured with a running catgut suture, and the perineal wound was partially closed with interrupted silk skin sutures. The middle third of the wound was left open around a corrugated rubber drain which drained the presacral space.

The drain was removed on the third postoperative day, and thereafter the wound was irrigated daily with a solution of hydrogen peroxide and loosely packed with gauze soaked in a 2·5 per cent solution of Milton.

Method 2. *Primary suture of perineum and pelvic peritoneum*: Two small suprapubic suction drains with multiple perforations were brought out extraperitoneally from the presacral space, and the pelvic peritoneum was closed with a running catgut suture. The presacral space was sprayed with a polymyxin–bacitracin aerosol, and the perineal wound was closed. Suture of the levator muscles was usually impossible, but the ischiorectal fat was approximated with interrupted chromic catgut sutures, and the perineal skin was closed with interrupted silk sutures. The suction drains were attached to rechargeable vacuum bottles after the abdomen was closed.

Method 3. *Primary suture of perineum and non-suture of pelvic peritoneum*: The pelvic peritoneum was not closed but, as in method 2, two small suprapubic suction drains were brought out from the presacral space. The perineal wound was closed in the same way as

---

* University Department of Surgery, The General Infirmary, Leeds.

Table I: COMPARISON OF THE THREE GROUPS OF PATIENTS WITH REGARD TO SEVERAL CLINICAL VARIABLES

	Method 1		Method 2		Method 3	
	No.	%	No.	%	No.	%
No. of cases	24		31		42	
Average age (yr±s.e.)	49·7 ±3·16		51·1 ±3·40		51·9 ±2·68	
Males	16	66·7	15	48·4	26	61·9
Females	8	33·3	16	51·6	16	38·1
No. of cases on systemic steroids	10	41·7	14	45·2	10	23·8
No. of cases with contamination of perineal wound	4	16·7	5	16·1	4	9·5
Nature of primary disease:						
Carcinoma	11	45·8	14	45·2	19	45·2
Crohn's disease	8	33·3	3	9·7	8	19·0
Ulcerative colitis	5	20·8	14	45·2	15	35·7
Type of surgery:						
Proctocolectomy	10	41·7	15	48·4	20	47·5
Abdominoperineal excision	14	58·3	16	51·6	22	51·5

Table II: HEALING OF THE PERINEAL WOUNDS

	Method 1		Method 2		Method 3	
Healing	No.	%	No.	%	No.	%
Perineal wound healed *per primam*	—	—	14	45·2	18	42·9
Perineal wound healed by 3 months	7	30·4	20	66·7	26	68·4
Perineal wound healed by 6 months	15	65·2	25	80·6	34	82·9

method 2 cases after spraying the presacral space with a polymyxin–bacitracin aerosol.

The patients treated by methods 2 and 3 were given ampicillin by intramuscular injection for 5 days after surgery. The suction drains were removed when they ceased to drain significant amounts of blood or serum, which was usually on the fourth or fifth postoperative day, and the perineal skin sutures were removed on the eighth postoperative day.

Allocation of patients to the trial

During the period of the study all patients undergoing rectal excision in the Professorial Surgical Unit, either as a separate operation or as part of a proctocolectomy, were considered for inclusion in the trial, but approximately two-fifths of them were rejected for three reasons.

a. In female patients having abdominoperineal excision for rectal cancer it was our invariable practice to excise the posterior vaginal wall along with the rectum. Because of the inability to provide a complete closure of the pelvic cavity from below after sacrificing the posterior vaginal wall, such patients were not included in the trial, two options of which would involve closure in this way. Instead patients from whom the posterior vaginal wall was removed with the rectum were treated electively by suture of the posterior three-quarters of the perineal wound, the pelvic cavity being drained by a strip of corrugated rubber inserted through the vaginal introitus and through the gap where the posterior vaginal wall had been.

b. If at the conclusion of the operation complete haemostasis in the pelvis could not be achieved by diathermy, ligature or suture, packing of the perineal wound with a gauze roll was necessary and the case was not entered in the trial.

c. If there had been *gross* contamination of the perineal wound during operation from associated fistulation or from laceration of the rectum during its removal, open drainage was preferred, rendering the case ineligible for incorporation in the trial.

Results

Numbers of patients included and allocation to the three methods

Altogether 106 patients were included in the trial; 57 treated by abdominoperineal excision of the rectum alone and 49 by proctocolectomy, the indications for the operations being carcinoma in 48 cases, ulcerative colitis in 37 cases and Crohn's disease in 21 cases.

The allocation of cases to the three methods of perineal wound management was 29 to method 1, 33 to method 2 and 44 to method 3.

Operative mortality

The overall operative mortality in the study was 8·5 per cent, but none of the 9 deaths could be definitely attributed to perineal wound complications.

Five patients died after method 1: 2 of advanced malignant disease, 2 of cardiorespiratory complications and the fifth of unexplained peritoneal sepsis and an intraperitoneal haemorrhage possibly related to systemic steroid therapy.

Two patients died after method 2: one from a massive pulmonary embolism and the other from a cerebrovascular accident.

Two patients died after method 3: both from peritonitis, in one case the result of colostomy necrosis and in the other from an unexplained perforation of the ileum. It is conceivable that the intraperitoneal drain used in the latter case may have caused pressure necrosis of the ileum.

Similarity of the groups of patients treated by the three methods

Excluding the 9 patients who succumbed during the early postoperative period, the numbers of patients available for study were 24 in method 1, 31 in method 2 and 42 in method 3.

Table I compares these groups with regard to age, sex, the incidence of systemic steroid therapy and operative contamination of the perineal wound, the nature of the initial disease and the type of operation performed. All the patients who were receiving systemic steroids and those who had received steroids within the 3 months prior to operation were given steroid cover during and after the operation.

It can be seen that there were some differences between the three groups with regard to several of these clinical variables. There were fewer females and more cases of Crohn's disease in method 1, and the incidence of systemic steroid therapy and operative contamination of the perineal wound was rather less in method 3 than in the other two methods. However, none of the differences between the three methods is statistically significant.

Perineal wound healing
Table II shows the data on the healing of the perineal wounds in the three groups of patients. It can be seen that there was no significant difference between the results obtained with the two methods of primary suture. Primary healing of the perineal wound occurred in 45·2 per cent of the patients in method 2 (suture of the perineum and pelvic peritoneum) and in 42·9 per cent of the patients in method 3 (suture of the perineum and non-suture of the pelvic peritoneum).

The results at 3 and 6 months respectively after operation showed that perineal wound healing was delayed in the open drainage method (method 1) compared with both methods managed by primary suture. Complete healing of the perineal wound at 3 months had occurred in only 30 per cent of the patients in method 1, whereas two-thirds of the wounds in methods 2 and 3 had healed by this time. Similarly, at 6 months healing had occurred in only 65 per cent of the wounds in method 1, whereas more than 80 per cent of the wounds in methods 2 and 3 had healed. However, these differences between the perineal wounds in method 1 and in methods 2 and 3 just fail to achieve statistical significance. Two patients are not included in the results at 3 and 6 months. One patient in method 3 had died of metastases and a patient in method 1 defaulted from the outpatients' clinic.

Morbidity
Table III shows the mean duration of stay in hospital for the patients in the three groups, and the incidence of postoperative ileus or intestinal obstruction and of further operations on the perineal wound.

The duration of stay in hospital was similar for each group and amounted to almost 4 weeks. Similarly, there was no significant difference between the three groups with regard to the incidence of ileus or obstruction, or further operations on the perineal wound.

For the purpose of the study, ileus was diagnosed if the patient failed to pass flatus or faeces by the fifth postoperative day, and intestinal obstruction was recorded when intestinal colic and vomiting required intravenous fluids and the cessation of oral intake. Approximately 20–30 per cent of patients developed ileus or obstruction according to these criteria, but no patient required a further laparotomy for these complications. The absence of a sutured pelvic peritoneum in method 3 patients did not result in a significant increase in the incidence of ileus or obstructive complications.

In method 1, 5 patients (20·8 per cent) required further operations on the perineal wound. In 3 cases the wound had to be packed within several hours of the original operation because of persistent bleeding, and 2 cases required exploration of the perineal wound for secondary haemorrhage during the second postoperative week. In method 2, 8 patients (25·8 per cent) developed a haematoma or abscess in the presacral space, and they required further surgical intervention. Similarly, 8 patients (19·0 per cent) in method 3 underwent further operations for septic complications in the perineal wound.

Table III: MEAN DURATION OF HOSPITAL STAY, INCIDENCE OF POSTOPERATIVE ILEUS OR INTESTINAL OBSTRUCTION AND FREQUENCY OF FURTHER OPERATIONS ON THE PERINEAL WOUND

	Method 1		Method 2		Method 3	
	No.	%	No.	%	No.	%
Average duration of stay in hospital (days ± s.e.)	27·6 ±2·23		27·4 ±1·95		27·7 ±1·51	
No. of cases of post-operative intestinal obstruction or ileus	6	25·0	6	19·4	12	28·6
No. of cases requiring further operations on the perineal wound	5	20·8	8	25·9	8	19·0

One patient in each of the two methods managed by primary suture of the perineal wound became seriously ill as a result of pelvic sepsis:

Case report (*method* 2): A 34-year-old female underwent proctocolectomy for ulcerative colitis. The operation was complicated by contamination of the perineal wound and the patient was receiving systemic steroids. On the third postoperative day she developed a swinging pyrexia, jaundice, thrombocytopenia and some degree of circulatory collapse. Inspection of the perineal wound revealed no external abnormality, and there was very little drainage from the presacral suction drains. Despite the normal appearance of the perineal wound it was felt that infection in the presacral space was the most likely explanation for the clinical features.

The patient was resuscitated and the perineal wound was explored. A large infected haematoma was evacuated from the space below the pelvic peritoneum. Her postoperative course was stormy, and a consumptive coagulopathy persisted for several days, but she went on to make a satisfactory recovery.

Case report (*method* 3): A 56-year-old woman underwent a rectal excision for ulcerative colitis. On the third postoperative day she developed spreading abdominal tenderness and vomiting, and examination revealed signs of peritonitis, maximal in the right iliac fossa. Inspection of the perineal wound revealed no external abnormality and there was little drainage from the presacral suction drains.

Laparotomy was performed and she was found to have a lower abdominal peritonitis with pus in the presacral space. The perineal wound was opened and packed, and she went on to make a satisfactory recovery, although ileus persisted for 10 days after surgery.

Factors affecting primary wound healing
Table IV shows the relationship between primary healing of the perineal wound and systemic steroid therapy, the nature of the underlying disease and operative contamination of the perineal wound. It can be seen that the only factor which had any significant bearing on the healing of wounds closed by primary suture was operative contamination of the wound. Contamination of the perineal wound with pus or faeces occurred in 9 cases, and none of these patients achieved primary wound healing. The difference between the healing of contaminated and uncontaminated perineal wounds is statistically significant ($\chi^2 = 4{\cdot}50$, $P < 0{\cdot}05$).

Table IV: RELATIONSHIP BETWEEN PRIMARY WOUND HEALING AND SYSTEMIC STEROID THERAPY, NATURE OF THE PRIMARY DISEASE AND OPERATIVE CONTAMINATION OF THE WOUND

	No. of cases	Healed *per primam*	% Primary healing
Systemic steroid therapy	24	10	41·7
No steroids	49	22	44·9
Nature of primary disease:			
Carcinoma	33	15	45·5
Ulcerative colitis	29	13	44·8
Crohn's disease	11	4	36·4
Operative contamination of perineal wound	9	0	0*
No contamination of perineal wound	64	32	50·0

* Significant incidence of failure in contaminated wounds ($\chi^2 = 4{\cdot}50$, $P \leq 0{\cdot}05$).

Table V: RELATIONSHIP BETWEEN UNHEALED WOUNDS AT 6 MONTHS AFTER SURGERY AND NATURE OF THE ORIGINAL DISEASE

Primary disease	No. of wounds unhealed	% Unhealed
Carcinoma	4	9·3
Ulcerative colitis	10	30·3*
Crohn's disease	7	36·8†

* Incidence of unhealed wounds in cases of ulcerative colitis significantly greater than that in carcinoma cases ($\chi^2 = 4{\cdot}47$, $P < 0{\cdot}05$).

† Incidence of unhealed wounds in cases of Crohn's disease significantly greater than that in carcinoma cases ($\chi^25 = \cdot63$, $P < 0{\cdot}02$).

Delayed wound healing

The total incidence of unhealed perineal wounds and persisting wound sinuses at 6 months after surgery was 22 per cent. *Table V* shows the relationship between this complication and the nature of the original disease. It can be seen that unhealed perineal wounds were significantly less common after operations for carcinoma by comparison with operations for Crohn's disease ($\chi^2 = 5{\cdot}63$, $P < 0{\cdot}02$) or ulcerative colitis ($\chi^2 = 4{\cdot}47$, $P < 0{\cdot}05$).

Discussion

In recent years a number of surgeons have recommended that the perineal wound following rectal excision should be closed by primary suture. Hultén et al. (1971), in a study of 36 patients managed by primary closure of the perineal wound, found that primary healing occurred in 75 per cent. Broader et al. (1974) reported that primary healing occurred in 63 per cent of 106 patients given primary closure, and Altemeier et al. (1974) claimed healing *per primam* in no less than 92 per cent of 125 patients with rectal cancer similarly managed. In the present study 44 per cent of primarily closed wounds healed by first intention.

The failures which have been recorded after primary closure of the perineal wound have been due to haematoma or abscess formation in the presacral space below the pelvic peritoneum (Hultén et al., 1971; Broader et al., 1974), and this was also our experience in the present study. It might have been expected that such troubles would be to a large extent avoided by th tion drainage to this site instituted by these three groups of workers and by ourselves, but presur the removal of blood from this space by sucti often less efficient than could be desired, partic if there is delay in commencing the suction at the clusion of the perineal dissection. We had cauti hoped that a further useful contribution to the sol of this problem might be provided by leaving th vic peritoneum unsutured in method 3, thus perm the small intestine to fall down into the pelvic and obliterate the presacral dead space. Howeve incidence of primary wound healing in the gro patients managed in this way in the present stud not significantly different from that which obt in the group in which the pelvic peritoneum sutured (*Table II*). Fortunately, the absence pelvic peritoneum did not result in an increase dence of postoperative obstructive complicatio ileus, but this method has the potential disadva that it may permit any sepsis arising in the pre space to spread upwards into the general perit cavity, as occurred in one case in the present On balance, therefore, we see no advantage in le the pelvic peritoneum unsutured.

Ruckley et al. (1970) described a method of pr closure of the perineal wound which incorpora pedicled graft of omentum in the space belo pelvic peritoneum, and they found that 8 out cases managed in this way achieved complete h of the perineal wound within 3 weeks of surger have no experience of this method but the reported by Ruckley et al. do not appear significantly better than those observed in the p study.

Another plan for dealing with the presacral sp connection with primary suture of the perineal would be to arrange for its periodic or constant tion as well as for suction, preferably using some tion, such as hyaluronidase or even streptokinas could help to dissolve any clot that might have fo We have so far had only minimal experience wi régime but we note that Schwab and Kelly (1974 used something similar with encouraging results

Several aspects were investigated in the p study in an effort to detect any systemic or local f which might adversely affect primary healing perineal wound. The use of systemic steroids cou be correlated with an increased incidence of w breakdown, nor was there any apparent corre between primary wound healing and the nature initial disease. However, there was a signifi higher incidence of failure in primarily closed w when operative contamination had occurred. tamination occurred in 9 of the wounds in our managed by primary closure, and none heale *primam*. Broader et al. (1974) also found that ope contamination had an adverse effect on the heal primarily closed wounds—in their study conta tion occurred in 15 wounds and only 5 of these *per primam*. These authors felt that primary clos contaminated perineal wounds was still indi presumably on the basis that no serious harm would result even if sepsis should occur, but we would strongly recommend that primary closure should not be performed if contamination of the perineal wound has taken place. In our experience primary wound healing is never achieved under these circumstances, and we have had one case in which serious septic complications ensued following primary closure of a contaminated perineal wound.

The average stay in hospital for the groups of patients managed by primary suture of the perineal wound was not significantly different from that of the group managed by open drainage. This similarity is not explained by a lengthy convalescence on the part of patients who required further operations on primarily closed wounds. Indeed, the need for further operations on the perineal wound did not seem to have any significant effect on the duration of stay. It appears that the duration of the period in hospital is principally related to the speed with which the patient attains the necessary confidence in the care of the ileostomy or colostomy. Thus, the average stay in hospital for the patients in all groups in the present study was about 4 weeks, irrespective of the methods used to manage the perineal wound.

Delayed healing of the perineal wound and persistent wound sinuses are troublesome complications which affect a significant proportion of patients following rectal excision. It is widely held that these complications are more common after operations for inflammatory diseases of the colon than after operations for carcinoma. In a study of 93 cases of ulcerative colitis treated by proctocolectomy, Watts et al. (1966) found that the incidence of unhealed wounds 6 months later was 25 per cent, and Jalan et al. (1969) recorded that the incidence of unhealed wounds in 106 cases of ulcerative colitis at 6 months after radical operation was 55 per cent. Lockhart-Mummery and Morson (1960) also stated that delayed healing of the perineal wound was a significant problem following rectal excisions for Crohn's disease, and Broader et al. (1974) found that the incidence of perineal sinuses 1 year after rectal excisions was four times greater in cases of Crohn's disease and ulcerative colitis than in cases of rectal carcinoma.

The present study has confirmed that perineal sinuses and unhealed perineal wounds are significantly more common after operations for Crohn's disease and ulcerative colitis compared with operations for carcinoma (*Table V*), but it was gratifying to find that the methods of primary wound closure used in the present study did not compound this problem. Indeed, persisting perineal sinuses were less commonly found in cases managed by primary suture of the perineal wound than in cases managed by open drainage.

It appears, therefore, that primary wound closure can be recommended as the most suitable management of the perineal wound following rectal excision, except for cases in which haemostasis in the pelvis has been incomplete or operative contamination has occurred. In our experience rather less than half the cases managed in this way heal *per primam*, but the wound complications which arise in the remainder are rarely of serious significance and convalescence is seldom prolonged. Furthermore, the subsequent healing of the perineal wound does not seem to be adversely affected when primary suture fails, and the incidence of persisting perineal sinuses and unhealed wounds in cases managed by primary wound closure is less than that which is encountered in cases treated by open drainage.

References

ALTEMEIER W. A., CULBERTSON W. R., ALEXANDER J. W., SUTURIUS D. and BOSSERT J. (1974) Primary closure and healing of the perineal wound in abdominoperineal resection of the rectum for carcinoma. *Am. J. Surg.* **127**, 215–219.

BROADER J. H., MASSELINK B. A., OATES G. D. and ALEXANDER-WILLIAMS J. (1974) Management of the pelvic space after proctectomy. *Br. J. Surg.* **61**, 94–97.

GABRIEL W. B. (1963) *The Principles and Practice of Rectal Surgery*, 5th ed. London, Lewis, p. 545.

GOLIGHER J. C. (1967) Treatment of carcinoma of the rectum. In: *Surgery of the Anus, Rectum and Colon*, 2nd ed. London, Baillière, Tindall & Cassell, pp. 609–775.

HAXTON H. (1970) *Surgical Techniques*. Bristol, Wright, pp. 121–122.

HULTÉN L., KEWENTER J., KNUTSSON U. and OLBE L. (1971) Primary closure of perineal wound after proctocolectomy or rectal excision. *Acta chir. Scand.* **137**, 467–469.

JALAN K. N., SMITH A. N., RUCKLEY C. V., FALCONER C. W. A., SMALL W. P. and PRESCOTT R. J. (1969) Perineal wound healing in ulcerative colitis. *Br. J. Surg.* **56**, 749–753.

LOCKHART-MUMMERY H. E. and MORSON B. C. (1960) Crohn's disease (regional enteritis) of the large intestine and its distinction from ulcerative colitis. *Gut* **1**, 87–105.

MILES W. E. (1908) A method of performing abdominoperineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon. *Lancet* **2**, 1812–1815.

MILES W. E. (1926) *Cancer of the Rectum*. London, Harrison, p. 60.

OATES G. D. and ALEXANDER-WILLIAMS J. (1970) Primary closure of the perineal wound in excision of the rectum. *Proc. R. Soc. Med.* (suppl.) **63**, 128.

RUCKLEY C. V., SMITH A. N. and BALFOUR T. W. (1970) Perineal closure by omental graft. *Surg. Gynecol. Obstet.* **131**, 300–302.

SCHWAB P. M. and KELLY K. A. (1974) Primary closure of perineal wound after proctectomy. *Mayo Clinic Proc.* **49**, 176–179.

WATTS J. MCK., DE DOMBAL F. T. and GOLIGHER J. C. (1966) Long-term complications and prognosis following major surgery for ulcerative colitis. *Br. J. Surg.* **53**, 1014–1023.

Br. J. Surg. Vol. 62 (1975) 292–294

Povidone-iodine for the control of surgical wound infection: a controlled clinical trial against topical cephaloridine

A. V. POLLOCK AND MARY EVANS*

SUMMARY

One hundred and ninety-two operation wounds in a general surgical practice were randomly allocated to receive either topical cephaloridine or a povidone-iodine spray, and the rate of wound sepsis was studied. In all types of operation cephaloridine proved superior to povidone-iodine as a prophylactic, the difference reaching a significant level in potentially contaminated wounds.

SEPSIS in a sutured surgical wound can cause suffering, economic hardship and, occasionally, serious illness or even death. Many methods have been advocated for the reduction of the rate of surgical wound infection and among these the application of topical antibiotics at the time of operation has stood the test of numerous controlled clinical trials (Evans et al., 1974).

Polk and Lopez-Mayor (1969), however, reported a significant lowering of their surgical wound sepsis rate by three doses of cephaloridine administered not topically but parenterally, and this work has been confirmed (Evans and Pollock, 1973).

Approaching the problem from a different direction, Gilmore and Martin (1974) have reported a significant reduction in the rate of sepsis in gridiron incisions for appendicectomy by a non-antibiotic application, namely povidone-iodine.

There is, naturally, a reluctance to use valuable therapeutic antibiotics for wound infection control because of the possibility of encouraging the emergence of resistant strains (Garrod, 1972). We have, therefore, tested in a randomly controlled clinical trial in a general surgical practice a povidone-iodine spray against topically applied cephaloridine, which has already been proved to be an effective prophylactic (Evans et al., 1974).

Patients and methods

Two hundred and six consecutive sutured surgical wounds (excluding wounds less than 3 cm in length and perineal wounds for abdominoperineal excisions of the rectum) were studied. The allocation to povidone-iodine spray or control (cephaloridine) was by the toss of a coin, and all the wounds were observed for at least 1 month. Fourteen patients who either received preoperative antibiotics or died within 4 weeks of operation without wound infection were excluded from the trial, leaving 192 wounds for analysis.

Povidone-iodine (Disadine DP, Avlex Ltd) is supplied as a dry powder in an aerosol can. It was sprayed into the wound during closure from a distance of 25 cm for 8 seconds. After the skin had been sutured the wound edges were again sprayed in the same way.

For the controls 1 g of cephaloridine (Ceporin, Glaxo Laboratories Ltd) was dissolved in 2 ml of water and instilled into the wound before skin closure, with care to avoid spillage.

In the majority of the potentially contaminated wounds a swab from the opened viscus or the infected lesion was sent for bacteriological examination, including cephaloridine sensitivity. Pus from most discharging wounds was cultured and the sensitivity of the organisms to cephaloridine determined.

In order to avoid observer bias the method of prophylaxis used was recorded on punch cards separate from the patient's notes. The significance of differences was assessed by calculation of χ^2.

Definitions

Primary wound sepsis is defined as 'a clear collection of pus which empties itself spontaneously or after incision' (Ljungqvist, 1964) and secondary sepsis as 'that which follows discharge from the wound of a substance other than pus' (Pollock, 1973). We recognize that it is possible for a wound discharging pus (and therefore primarily infected) to acquire a secondary infection as well, but this has not altered the classification of that infection as primary.

A wound which discharged fluid within 4 weeks of operation was regarded as septic unless the discharge was merely of serum or lymph, was sterile and rapidly ceased. Although some wound swabs were reported to be sterile, if the discharge was obviously pus the wound was classified 'septic'.

We have classified wounds as 'clean' (in which there is no likelihood of endogenous bacterial contamination) and 'potentially contaminated' (in which this exists to a greater or lesser degree—we have recognized once again the higher incidence of wound sepsis with colorectal surgery including perforated appendicitis).

Results

One hundred and ninety-two wounds were studied. Eighty-six received cephaloridine and 106 povidone-iodine spray.

Primary infections

Four wounds discharged pus in the cephaloridine group (5·1 per cent) and 19 in the povidone-iodine group (17·9 per cent). Both in clean and in potentially

---

* Scarborough Hospital, Scarborough, Yorkshire.

Table I: COMPARISON OF WOUND INFECTIONS IN THE CEPHALORIDINE AND POVIDONE-IODINE GROUPS

	Cephaloridine			Povidone-iodine		
	Total wounds	Primary sepsis	Secondary sepsis	Total wounds	Primary sepsis	Secondary sepsis
Clean						
Head and neck	2	0	0	6	0	1
Breast and axilla	4	0	1	4	0	1
Laparotomy	7	0	0	5	1	0
Lumbar	4	0	0	5	0	0
Groin hernias and varicose veins	24	0	0	28	1	0
Arterial—lower limb	5	0	1	4	0	1
Amputations—lower limb	3	0	0	1	0	0
Total clean	49	0 (0%)	2 (4·1%)	53	2 (3·8%)	3 (5·7%)
Potentially contaminated						
Stomach	5	3	1	11	4	2
Gallbladder	7	0	0	17	8	2
Gridiron appendicectomy	11	0	0	14	3	0
Bladder	6	0	0	4	0	2
Kidney	1	0	0	1	0	0
Infected lesions	1	0	0	1	0	0
Colorectal and perforated appendicitis	6	1	1	5	2	1
Total potentially contaminated	37	4 (10·8%)	2 (5·4%)	53	17 (32·1%)	7 (13·2%)

The difference between the primary sepsis rates in potentially contaminated wounds is significant ($\chi^2 = 5{\cdot}5$, $P < 0{\cdot}02$).

Table II: ORGANISMS CULTURED FROM SEPTIC WOUNDS

	Primary sepsis		Secondary sepsis	
Organisms	Clean	Potentially contaminated	Clean	Potentially contaminated
Staphylococci	2	6	3	6
Intestinal organisms	0	10	1	3
Pus sterile or not sent	0	5	1	0

contaminated wounds the sepsis rate was higher with povidone-iodine than with cephaloridine (*Table I*), but the difference reached statistical significance only in the potentially contaminated group ($\chi^2 = 5{\cdot}5$, $P < 0{\cdot}02$), and the trial was therefore stopped for ethical reasons.

In the majority of cases (3 out of 4 with cephaloridine and 11 out of 19 with povidone-iodine) the wound sepsis was of minor importance—a stitch abscess or its equivalent. Twelve wounds discharged pus during the first 7 days after operation and 11 on the eighth day or later, the longest interval being 31 days.

In 66 of the 90 potentially contaminated cases in this series an operation swab was cultured, and an organism was found in 37. Eight were staphylococci, sensitive to cephaloridine, and 29 were intestinal organisms all but 3 of which were sensitive to cephaloridine. In the 29 cases in which the operation swab was sterile, wound sepsis developed in 6 (21 per cent). When an organism was cultured at operation, 12 out of the 37 wounds subsequently discharged pus (33 per cent). This difference lacks statistical significance ($\chi^2 = 1{\cdot}13$, $0{\cdot}30 > P > 0{\cdot}20$). Whether or not the operation swab was sterile, wounds were less likely to become septic when cephaloridine was used for prophylaxis than when povidone-iodine was the agent employed (3 out of 25 compared with 15 out of 41, $\chi^2 = 4{\cdot}73$, $P < 0{\cdot}05$).

When we came to correlate the bacteriology at operation with that of pus from the 23 primarily infected wounds, we found that in 15 cases one of the swabs was sterile or had not been taken. Of the remaining 8, the pus subsequently cultured from 5 of the wounds yielded an organism apparently identical with that found at operation, and in 3 the organism differed from the one previously cultured.

Secondary infections

In 4 of the 86 patients receiving cephaloridine (5·1 per cent) and 10 of the 106 patients receiving povidone-iodine spray (9·4 per cent) secondary wound sepsis developed (*Table I*). This difference is not significant ($\chi^2 = 1{\cdot}60$, $0{\cdot}30 > P > 0{\cdot}20$).

Of these 14 patients, the initial discharge in 5 was of peritoneal fluid associated with an intraperitoneal drain (3) or a burst abdomen (2). In 2 patients the first discharge was of serum from a haematoma and in 2 of lymph from the groin after operation on the femoral artery. Four patients developed secondary sepsis after other fistulas (2 urinary, 1 biliary and 1 salivary), and one arose as a result of ischaemic sloughing of a wound edge.

Five of these secondary infections arose in clean wounds, and 9 in potentially contaminated wounds. In only one was the organism cultured from the wound the same as that cultured at operation. There was, therefore, no correlation between the nature of bacterial contamination at operation and subsequent secondary wound infection.

Discussion

Most primary wound infections occur during surgery from endogenous sources (due to opening of potentially contaminated hollow muscular viscus or excision of an infected lesion). Provided that normal aseptic precautions are taken, contamination from exogenous sources such as the operating theatre air, surgeons' hands or unsterile instruments is exceedingly uncommon (Report, 1964; Davidson and Smith, 1969; Davidson et al., 1971). The rare primary infections after clean operations are usually explicable by contamination from the patient's nose or skin or by haematogenous seeding (Howe, 1968).

Secondary wound sepsis, on the other hand, does not arise as a result of infection of the wound during operation and cannot be prevented by applying antibacterial substances to the wound. This prophylaxis depends on the prevention of haematomas and fistulas and the avoidance of cross-infection in the ward. It is in this connection that the currently accepted ward architecture of small rooms, individually ventilated, is so important (Smith et al., 1974). It is almost impossible in a large multi-bedded ward to maintain the sterility of a discharging wound. *Table II* shows that the predominant organism in primary wound infections is intestinal, whereas staphylococci are commoner in secondary infections.

In the present trial cephaloridine proved to be much more efficient than povidone-iodine in the prevention of primary wound infections. Secondary infections also were commoner with povidone-iodine, and this may reflect an irritative property of this substance leading to effusion of serum which subsequently discharges and becomes infected.

Our very unsatisfactory results with povidone-iodine contrast with those reported by Gilmore and Martin (1974), whose trial was confined to gridiron appendicectomies. In their series, excluding cases of perforated appendicitis, 15 out of 136 (11·0 per cent) in the control group discharged pus compared with 6 out of 135 (4·4 per cent) in the povidone-iodine group ($\chi^2 = 4 \cdot 11$, $P < 0 \cdot 05$). One has to postulate only a single missed infection in the latter group to reduce χ^2 to 3·10 and remove the statistical significance.

In the present series no grid iron appendicectomy wounds out of 11 discharged pus in the cephaloridine group compared with 3 out of 14 which received povidone-iodine. This difference by itself cannot be significant and it is only when the sepsis rate of all potentially contaminated operations is considered that cephaloridine emerges as a significantly better prophylactic agent than povidone-iodine.

Despite the theoretical danger of the encouragement of resistant organisms by the local use of a potent systemic antibiotic for wound infection prophylaxis, the present trial demonstrates that this must continue to be our practice until an equally effective alternative is available.

References

DAVIDSON A. I. G., CLARK C. and SMITH G. (1971) Postoperative wound infection: a computer analysis. *Br. J. Surg.* **58**, 333–337.

DAVIDSON A. I. G. and SMITH G. (1969) Bacteriological studies in the operating theatre in relation to postoperative wound sepsis. *Br. J. Surg.* **56**, 705.

EVANS C. and POLLOCK A. V. (1973) The reduction of surgical wound infections by prophylactic parenteral cephaloridine. *Br. J. Surg.* **60**, 434–437.

EVANS C., POLLOCK A. V. and ROSENBERG I. L. (1974) The reduction of surgical wound infections by topical cephaloridine: a controlled clinical trial. *Br. J. Surg.* **61**, 133–135.

GARROD L. P. (1972) Causes of failure in antibiotic treatment. *Br. Med. J.* **4**, 473–476.

GILMORE O. A. J. and MARTIN T. D. M. (1974) Aetiology and prevention of wound infection in appendicectomy. *Br. J. Surg.* **61**, 281–287.

HOWE C. W. (1968) Experimental wound sepsis from transient *Escherichia coli* bacteremia. *Surgery* **66**, 570–574.

LJUNGQVIST U. (1964) Wound sepsis after clean operations. *Lancet* **1**, 1095–1097.

POLK H. C. jun. and LOPEZ-MAYOR J. F. (1969) Postoperative wound infection: a prospective study of determinant factors and prevention. *Surgery* **66**, 97–103.

POLLOCK A. V. (1973) Wound infection in acute appendicitis. *Lancet* **2**, 1384.

REPORT (1964) Report of an Ad Hoc Committee of the Committee on Trauma, Division of Medical Sciences, National Academy of Sciences–National Research Council: Postoperative wound infections. *Ann. Surg.* **160**, Suppl., 1–192.

SMITH G., LOGIE J. R. C., MACDONALD A. and SMYLIE H. G. (1974) Ward design in relation to postoperative wound infection: part III. *Br. Med. J.* **3**, 13–15.

Br. J. Surg. Vol. 62 (1975) 295–297

Bacteria in flower vase water: incidence and significance in general ward practice

C. A. BARTZOKAS, MARGUERITE P. HOLLEY AND CHRISTINE A. SHARP*

SUMMARY

Culture of flower vase water from wards in the David Lewis Northern Hospital, Liverpool, revealed large numbers of potentially pathogenic bacteria. The types of organisms isolated may reflect the particular ecology of this hospital as they differed in some ways from those reported from other centres. The incidence of wound infections during the period of study was low (5·2 per cent) despite the regular overgrowth of bacteria in flower vases, and there did not appear to be any definite correlation between the types of bacteria isolated from flower vase water and those responsible for wound infections.

The addition of hydrogen peroxide to flower vases proved a very effective antiseptic and is recommended for general use as a precautionary measure.

There have been several conflicting reports on the potential hazard in hospital practice of bacteria growing in flower vase water. Thus, whereas Watson and Koons (1973) considered that *Pseudomonas aeruginosa* cultured from ornamental flowers may be responsible for some hospital infections, Schroth et al. (1973) indicated that definite proof of pathogenicity was lacking despite the fact that 50 per cent of the strains of *Pseudomonas* isolated from plants had similarities to human ones. Furthermore, Hughes (1974) considered that flowers in hospital wards were probably the victims rather than the source of human bacterial infections. On the other hand, Taplin and Mertz (1973) concluded that the growth of Gram-negative bacteria in flower vase water may be responsible for the transmission of hospital infections, and Ansorg et al. (1974) reported a case of septicaemia due to *Erwinia* spp. which led to the death of a debilitated patient.

The problem of bacterial overgrowth in flower vase water needs therefore to be reassessed, and several studies in different hospital environments are required before a true picture of its exact significance can be ascertained. For these reasons we decided to investigate the problem at the David Lewis Northern Hospital, where over a period of 6 months cultures were made of the flower vase water from wards and a record kept of the incidence and bacteriology of all postoperative wound infections during the same period of time.

Materials and methods

In this hospital the flowers usually given to patients consist of carnations, chrysanthemums, freesias, lilies of the valley, marguerites, roses and tulips. Cut flowers are put into vases containing 1 litre of tap water and changed at the sink in the sluice daily by the ward orderlies.

The bacterial flora of water from flower vases was initially studied. Samples were taken from 60 vases in 9 general wards at this hospital. Before sampling, the flowers were gently agitated and 5 ml of the flower water were transferred with a sterile Pasteur pipette to a sterile container. Within 1 hour of sampling the water was inoculated on to Oxoid MacConkey agar and blood agar plates, using a standard platinum wire loop. No addition of sodium thiosulphate (to eliminate chlorine residues) was made to the culture media, as Taplin and Mertz (1973) reported no significant difference in results with and without this substance. The plates were incubated for 24 hours at 37 °C and for a further 24 hours at room temperature (17–25 °C). In addition the tap water and swabs from the inside of the water taps in the wards were cultured in a similar way. The bacterial growth was then assessed by visual means as 'heavy', 'moderate' or 'light'. Colonies were subcultured whenever it was deemed necessary. Medical bacteria were identified by Gram reaction, morphology, spores, motility, catalase, oxidase, O–F tests, carbohydrate breakdown, ability to grow in air and secondary tests, as described by Cowan and Steel (1966).

In order to study the effect of hydrogen peroxide a further 7 vases from the same ward environment were sampled by the same method and cultured on to MacConkey agar. Further cultures were made 1, 2, 8, 24 and 48 hours after the addition of 50 ml of 10 volumes hydrogen peroxide to each vase. The flowers were left for 72 hours in the same water to see if the added hydrogen peroxide in any way affected the state of the flowers.

In another experiment powdered maganese dioxide was added to the culture media before plating the inocula of further flower vase water previously treated with hydrogen peroxide. Manganese dioxide was included as a neutralizer of H_2O_2 to ensure that the latter was not inhibiting bacterial growth in the culture medium.

The incidence and bacteriology of postoperative wound infections were analysed during the period of study. The wards in this hospital are of the open Nightingale type. Wound sepsis was accepted only when culture from the wound or its discharge was positive for pathogens. The operations were classified as 'clean', e.g. thyroidectomies, 'potentially infected', where there was a risk of contamination during

---

* David Lewis Northern Hospital, Liverpool.

Table I: INFECTED OPERATION WOUNDS

Operations	No. of cases	
Clean operations		19
Laparotomy only	4	
Vagotomy and drainage	4	
Cholecystectomy	3	
Thrombo-endarterectomy	2	
Femoropopliteal bypass	1	
Nephrectomy	1	
Repair of inguinal hernia	1	
Oophorectomy and adrenalectomy	1	
Excision of basal cell carcinoma	1	
Partial thyroidectomy	1	
Potentially infected operations		19
Appendicectomy	9	
Abdominal resection	4	
Colectomy	2	
Refashioning colostomy	1	
Laparotomy and colostomy	1	
Reduction of strangulated inguinal hernia	1	
Radical gastrectomy	1	
Infected operations		8
Perforated appendicitis	2	
Pilonidal sinus	2	
Opening and exploration of perineal wound	1	
Incision of abscess	1	
Necrotic infarction of gut	1	
Perinephric abscess	1	

Table II: ORGANISMS ISOLATED FROM POSTOPERATIVE WOUND INFECTIONS

	Type of operation			
Organism	'Clean'	'Potentially infected'	'Infected'	Total
Single culture				
E. coli	4	5	1	10
Staph. aureus	7	2	—	9
Proteus spp.	4	1	3	8
Staph. albus	2	3	—	5
Bacteroides	—	3	—	3
Diphtheroides	1	1	—	2
Str. pneumoniae	1	—	—	1
Mixed culture				
E. coli+*Proteus* spp.	—	2	1	3
E. coli+Bacteroides	—	1	—	1
E. coli+*Ps. aeruginosa*	—	—	1	1
E. coli+*Staph. aureus*	—	—	1	1
E. coli+yeasts+haemolytic streptococcus (group F)	—	1	—	1
E. coli+*Clostridium oedematiens*+yeasts +*Staph. albus*+*Sphaerophorus necrophorus*	—	—	1	1
Total	19	19	8	46

operation, e.g. operations on the gastro-intestinal tract distal to the upper jejunum, and 'infected', including operations carried out in the presence of established sepsis, e.g. drainage of abscesses and surgery for peritonitis, etc.

Results

Flower vase water with no additives

A heavy growth of mixed bacteria was obtained from all 60 samples studied from the 9 wards during a period of 6 months. There was an overall predominance of *Escherichia coli* and the Enterobacter/Klebsiella group of organisms. No *Proteus* or *Pseudomonas* spp. were isolated. The tap water and swabs from the taps showed a scanty growth of saprophytic bacteria only.

Effect of hydrogen peroxide

A moderate to heavy mixed growth of organisms was initially obtained from 7 vases which were subsequently treated with hydrogen peroxide. There was no growth in 35 samples taken from the same vases at intervals of 1–48 hours after treatment with hydrogen peroxide. The addition of hydrogen peroxide to the water produced no detrimental effect on the flowers.

Effect of manganese dioxide

A similar growth inhibition was obtained in hydrogen-peroxide-treated specimens even when manganese dioxide was added to the culture media.

Postoperative wound infections

During the course of the study there was a total of 46 postoperative wound infections (*Table I*) out of a total of 880 operations. The organisms isolated are shown in *Table II*.

Discussion

The present study shows an alarming incidence of bacterial growth in flower vases in this hospital. The most common organisms grown were *Escherichia coli* and those of the Enterobacter/Klebsiella group.

It is interesting that, contrary to previous reports, neither *Proteus* nor *Pseudomonas* spp. were cultured on any occasion during the course of this study. This may be a reflection of the bacterial ecology of this hospital. Despite the heavy growth of bacteria from flower vase water from surgical wards we encountered an overall incidence of postoperative wound infections of only 5·2 per cent. The three most common organisms cultured from postoperative wounds were *E. coli*, *Staphylococcus aureus* and *Proteus* spp. which respectively accounted for 1·13, 1·02 and 0·9 per cent of infections. We did not type the *E. coli* from the flower vase water or those isolated from wound infections and it is possible they were of the same strain. However, the general lack of correlation between the bacterial flora of flower vase water and that cultured from postoperative wounds, together with the low incidence of wound infections encountered during the period of study, argues against flower vase water being responsible for the production or transference of wound infections. Indeed in this hospital where flower vase bacteria were routinely grown during the period of study, the incidence of postoperative wound infection was well below the national average of 9·7 per cent reported by the Public Health Laboratory Service (1960). It must, of course, be stressed that the patients we studied had no evidence of depressed resistance to infections, and certainly none of the infections could be classed as opportunistic in nature. It is conceivable, and indeed likely, that flower bacteria may produce serious infections in severely debilitated patients and this has been reported (Ansorg et al., 1974). In any event the addition of hydrogen peroxide results in effective decontamination of flower vase water and we recommend the addition of this chemical as a precautionary measure.

Treatment of flower vase water with antiseptics has previously been reported (Smellie and Brinklow, 1963; Johansen et al., 1974). Our studies have confirmed the preliminary reports of Rosenzweig (1973) in that hydrogen peroxide was found to be very effective in preventing the growth of bacteria in flower vase water. The results obtained when manganese dioxide was added to the culture media indicates that growth inhibition was not due to any direct action of hydrogen peroxide in the culture media itself.

References

ANSORG R., THOMSSEN R. and STUBBE P. (1974) *Erwina* species causing fatal septicaemia in the newborn. *Med. Microbiol. Immunol. (Berl.)* **159**, 161–170.

COWAN S. T. and STEEL K. J. (1966) *Manual for the Identification of Medical Bacteria.* Cambridge, Cambridge University Press.

HUGHES W. H. (1974) Protecting chrysanthemums from hospital infections. *Lancet* **1**, 267–268.

JOHANSEN K. S., LAURSEN H. and WILHJELM B. J. (1974) Flower vases as reservoirs of pathogens. *Lancet* **1**, 359.

PUBLIC HEALTH LABORATORY SERVICE (1960) Incidence of surgical wound infection in England and Wales. *Lancet* **2**, 659–663.

ROSENZWEIG A. L. (1973) Contaminated flower vases. *Lancet* **2**, 568–569.

SCHROTH M. N., CHO J. J. and KOMINOS S. D. (1973) No evidence that Pseudomonas on chrysanthemums harms patients. *Lancet* **2**, 906–907.

SMELLIE H. and BRINKLOW P. (1963) The use of antiseptics for delaying decomposition of cut flowers in a hospital ward. *Lancet* **2**, 777–778.

TAPLIN D. and MERTZ P. (1973) Flower vases as reservoirs of pathogens. *Lancet* **2**, 1279–1281.

WATSON A. G. and KOONS C. E. (1973) Pseudomonas on the chrysanthemums. *Lancet* **2**, 91.

Br. J. Surg. Vol. 62 (1975) 298–302

Analgesic abuse in urological practice

R. W. PARKER AND RICHARD E. SHAW*

SUMMARY

Thirty-three patients seen in a urological department had taken large doses of analgesic for prolonged periods of time. In 9 cases a diagnosis of pyramidal necrosis was established, while 4 others had pyelographic evidence of pyelonephritis, and analgesic abuse was probably an important aetiological factor in their renal condition. Analgesic nephropathy is easily overlooked unless patients are questioned routinely regarding their intake of analgesic. It is important to identify the group of patients without evidence of serious renal disease who are taking excessive quantities of analgesic and to urge them to abandon the practice.

PAPILLARY necrosis was first described in 1877 by Von Friedreich who observed the condition in association with obstructive uropathy caused by prostatic hypertrophy. As further cases were reported links with acute pyelonephritis, diabetes mellitus and obstruction in the urinary tract were established. In Switzerland Spühler and Zollinger (1953) described an autopsy series of 30 patients afflicted with a condition which they termed 'interstitial nephritis', and which was associated with consumption of phenacetin-containing analgesics. In 22 out of 30 cases there was papillary necrosis, but there was no incidence of diabetes or of urinary obstruction. Since then a substantial number of papers have appeared dealing with 'analgesic nephropathy', as the condition has come to be known, although by 1970 only 44 cases had been reported in England and Wales (Koutsaimanis and de Wardener, 1970).

Patients

During the years prior to 1973, 9 cases of analgesic nephropathy received treatment in the Urological Department at Walsgrave Hospital, Coventry, and the details of these cases are analysed below. In addition, 24 patients were seen who had taken excessive amounts of analgesics for prolonged periods of time, and this group will receive examination later in the paper.

Analgesic nephropathy (*Table I*)

Sex and age

Of the 9 cases, 8 were female, giving a female to male ratio of 8 : 1. This is in harmony with general experience of this disorder. The age at the time of presentation varied from 24 to 66 years, with an average of 53 years. De Wardener (1973) stated that the diagnosis is usually made around the age of 50.

Presenting symptoms

The 9 patients presented with symptoms of a varied nature. Two were admitted in renal failure, 7 had symptoms of infection such as dysuria, frequency and haematuria and 1 was admitted with septicaemia. Four complained of renal pain or had actual ureteric colic, and 1 of these patients passed necrotic papillae in the urine. The length of the clinical history varied from 1 month to 9 years with an average of 22 months, but of course the history of analgesic intake was much longer, being from 8 to 30 years with a mean of 14 years.

Amount of analgesic consumed

An attempt was made to estimate the total amount of analgesic taken—not an easy task because of the vagueness of the history, and in some cases an element of deliberate concealment. The results are shown in *Table I* and indicate a wide variation. At one extreme only 0·6 kg of phenacetin was taken, while at the other, consumption was 39 kg each of aspirin and phenacetin (*Case* 7) which corresponds to 100–150 tablets of codeine per week for 20 years. Fortunately, intake of this order does not necessarily lead to renal damage. We have records of a patient with ankylosing spondylitis who took 6–9 Phensic tablets daily for 28 years; at the end of this time his intravenous pyelogram was normal and the creatinine clearance 110 ml/min. His wife included a bottle of tablets in her weekly shopping list. De Wardener (1973) said the amount of phenacetin needed to produce radiological changes varied from 1 to 25 kg taken for a period of from 2 to more than 20 years.

Clinical features

Urinary infection

Infection of the urinary tract was present in all our cases, the responsible organism being coliforms in 5 instances, *Proteus* sp. in 3 and *Streptococcus viridans* in 1. The infection often proved resistant to treatment. The incidence of infection has varied widely in different reports. Patients may present with sterile pyuria; in fact some authors have found analgesic nephropathy to be a more frequent cause than tuberculosis of this urinary abnormality.

Anaemia

All the patients had reduced haemoglobin levels. In 5 cases the anaemia was severe, with values between 6·0 and 7·5 g per cent. As might be expected, this group included those with the heaviest intake of analgesic. A high incidence of anaemia has been noted in other reported series of cases. The anaemia is iron-deficient in type and important factors in its genesis include the effect of aspirin on

---

* Walsgrave Hospital, Walsgrave-on-Sowe, Coventry.

Table I: DETAILS OF THE CASES OF ANALGESIC NEPHROPATHY

	Drugs								Renal function		
Case	Name	Dose (tablets/wk)	Time (yr)	Total phenacetin intake (kg)	Reason	Blood pressure (mm Hg)	MSU culture	Haemoglobin (g %)	SU (mg %)	SC (mg %)	CC (ml/min)
1. C. P. (64, M)*	Antoin	42	25	10·9	Arthritis	180/100	*E. coli*	11·2	47	1·8	39
2. I. S. (54, F)	Codeine	30	9	3·5	Headache	160/100	*Proteus* sp.	10·4	62	2·2	24
3. N. W. (58, F)	Codeine	42	15	8·2	Arthritis	150/80	*E. coli*	7·7	49	—	—
4. W. P. (65, F)	Various	42	20	5·7	Headache	180/100	*E. coli*	10·2	124	3·8	9
5. F. W. (53, F)	Codeine	25	10	3·9	Nervous trouble	130/70	*Proteus* sp. *E. coli*	7·4	58	2·1	32
6. R. P. (66, F)	Antoin	42	12	5·3	Generalized pains	?	*Proteus* sp.	8·4	108	2·8	37
7. M. D. (38, F)	Codeine	275	3	39·0	Generalized pains	230/140	*E. coli*	6·4	42	1·5	71
8. I. M. (56, F)	APC	42	30	16·4	Headache	210/100	*Proteus* sp.	7·5	332	—	8
9. P. R. (24, F)	Phensic	15	8	0·6	Headache	110/60	*E. coli*	11·1	36	0·9	92

MSU, Midstream specimen of urine. SU, Serum urea. SC, Serum creatinine. CC, Creatinine clearance. APC, Aspirin, phenacetin and caffeine.
* (Age, sex).

the gastrointestinal tract and poor renal function. In several of our cases the erythrocyte sedimentation rate was elevated.

Hypertension

In 5 patients the diastolic pressure was over 90 mm Hg and 2 of the patients had moderately severe hypertension. In 1 patient the blood pressure rose rapidly from 150/90 to 230/140 in the course of 3 months following the diagnosis of the condition. Another became hypertensive about 2 years after analgesic nephropathy had been diagnosed and the intake of analgesic had been abandoned. The reported incidence of hypertension varies from 33 to 75 per cent.

Renal function

Two patients were suffering from frank renal failure when first seen, but in 5 others reduced renal function was shown by a raised blood urea, reduced creatinine clearance or both. The incidence of severe renal impairment varies a good deal in different series and is probably related to variations in the sources of material. The earliest defects in renal function are loss of the ability to concentrate urine due to destruction of medullary tissue, and inability to excrete an acid load.

Psychological disturbance

Four of our 9 patients had evidence of mental abnormality. One suffered from chronic alcoholism, another was a regular attender at hospital with unexplained symptoms and 2 volunteered that they suffered considerably from nervous trouble. With increasing experience of the disorder, we came to recognize a rather withdrawn type of personality associated with the syndrome. Gault et al. (1968) found that one-third of his patients had had psychiatric treatment, mainly for anxiety, marital disharmony, depression drug-taking other than analgesics and alcoholism. Murray et al. (1970) commented that analgesic nephropathy was uncommon among psychotics, but associated with neurosis.

Peptic ulceration

One patient had undergone partial gastrectomy for benign gastric ulcer which had presented 3 years after the abuse had started but 12 years before the onset of renal symptoms, while another had a long history of dyspepsia and had suffered several haematemeses, although no ulcer was demonstrated by barium studies. Dawborn et al. (1966) have discussed the association of peptic ulceration, chronic renal disease and analgesic abuse, and found peptic ulceration present in 30 out of 92 cases of papillary necrosis due to excessive intake of analgesics. Peptic ulceration, or the aggravation of pre-existing ulceration, may be attributed to the aspirin rather than the phenacetin intake, and is not found in the patients who have not taken aspirin as part of the analgesic intake (Gault et al., 1968).

Radiological diagnosis

Confirmation of the diagnosis of analgesic nephropathy depends upon pyelographic evidence of renal change. In our early cases poor renal function frequently prevented us from obtaining good intravenous pyelograms, and retrograde pyelography or ascending ureterography was needed. More recently, the use of high dose urography has facilitated the detection of renal abnormalities, but we still find the ascending ureteropyelogram affords the best pictures. The early signs of disease are poor concentration of dye in the calices, widening of the caliceal fornices due to papillary shrinkage, irregularity of papillary outline and offshoots of the dye into the papillae, indicating their early separation. Later signs are the presence of medullary cavities of various sizes (*Fig.* 1), ring shadows caused by sloughs lying in dye-filled cavities (*Fig.* 2),

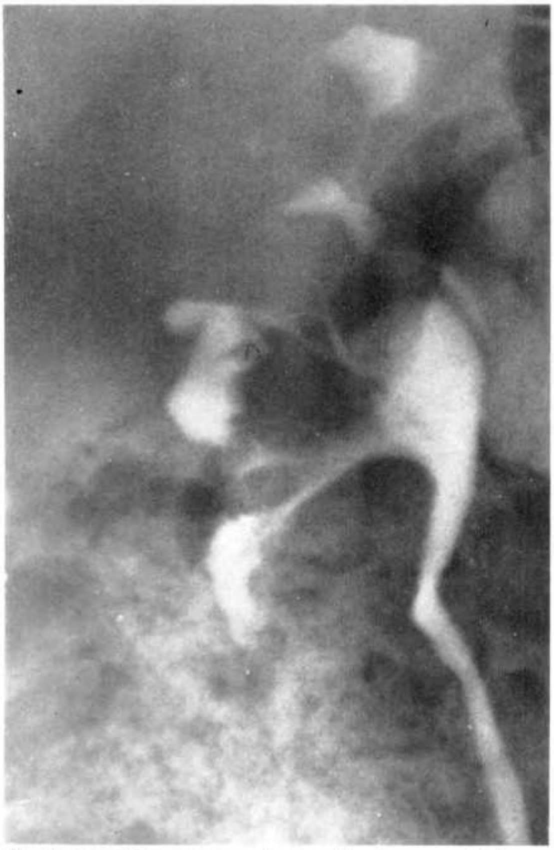


Fig. 1. Ascending ureteropyelogram showing pyramidal necrosis. Multiple cavities of irregular outline are visualized.

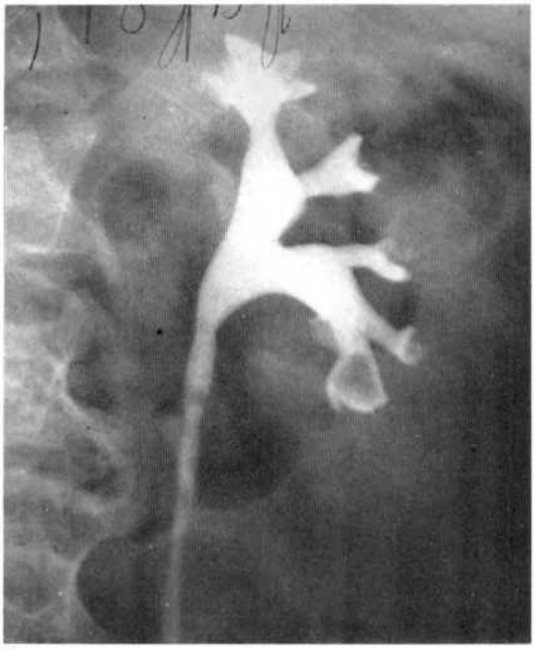


Fig. 2. Ascending ureteropyelogram showing pyramidal necrosis. A pyramid in the lowest calix has separated completely.

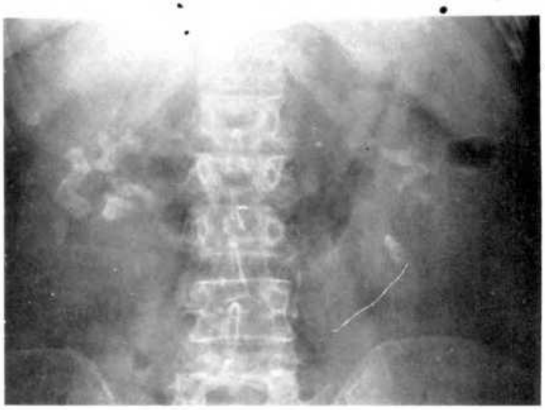


Fig. 3. Renal calculi secondary to pyramidal necrosis showing characteristic translucent centres.

calcification of papillae and finally shrinkage of the kidneys. The necks of the calices often appear elongated (*Fig.* 1). Lindvall (1960) found that papillary calcification only occurred in the presence of sloughing of the papillae and urinary infection with *Proteus* sp., and that 'without these factors stone formation was very rare'. Further deposits of calcium lead to the formation of calculi with radiotranslucent centres, producing a characteristic appearance (*Fig.* 3). Surgeons should be on the look-out for this type of stone and seek a history of analgesic abuse from the patient. In 6 of our 9 cases medullary cavities were shown. In one case papillary calcification was observed and another patient had multiple calculi with translucent centres. A reduction of the overall size of the kidneys or localized cortical thinning was noted in 3 cases. Two showed filling defects caused by sloughing of pyramidal tissue.

Reason for excessive analgesic intake

Two patients had legitimate reasons for taking analgesics, namely suffering from arthritis. The remainder took tablets for 'migraine' (although none suffered from true migraine), headaches or indefinite generalized pains. Several patients were vague about their reasons and were reluctant to volunteer information; they seemed unable to appreciate the irrationality of taking a drug day after day for intermittent symptoms such as headache. One was left with the impression that they obtained a sense of uplift and well-being from taking the tablets. A knowledge of medical matters did not preclude addiction, since one of the 9 cases was a qualified midwife and another was a nurse and the wife of a medical practitioner. Prescott (1966) found headache the commonest reason for addiction and arthritis the second most frequent. Dawborn et al. (1966) gave first place to headache, with psychological upset as the next most frequent cause, while factory workers reported by Nordenfelt and Ringertz (1961) took powders to increase their concentration at work.

Concealment

Patients indulging in analgesic abuse are usually very unwilling to admit to their addiction. One must be prepared to sit down with the patient and gently, but remorselessly drag out the details. Whether from shame or suppression of the facts into the unconscious, they have immense difficulty in providing information regarding the duration of intake, frequency of self-administration and the daily or weekly dose. In time, one usually establishes a satisfactory picture, but even so, the assessments of the total intake of tablets by our patients were almost certainly underestimates.

Diagnosis

A typical case of analgesic nephropathy is a middle-aged woman with psychological problems complaining of symptoms of persistent and often severe urinary infection with signs of impaired renal function and anaemia. Dyspeptic symptoms may also be present. The initial diagnosis is often chronic pyelonephritis, but a history of excessive analgesic intake alerts the surgeon who may then find in the pyelographic studies evidence of destruction of medullary tissue as shown by one or more of the signs described above. As de Wardener (1973) puts it, 'the diagnosis is made by asking the right questions'. Unlike chronic pyelonephritis, the disease is always bilateral. The type of case most easily diagnosed is the patient who passes in the urine one or more sloughing pyramids which can then be indentified histologically. The type of pyramidal necrosis associated with diabetes runs a more acute course and is less common than analgesic nephropathy—we have seen only 2 cases during the same period.

Treatment

The treatment of analgesic nephropathy involves: (1) withdrawal of phenacetin, (2) treatment of urinary tract infection, (3) treatment of renal failure, if present, and (4) in some cases, surgical removal of obstructing pyramidal tissue.

The most important element in treatment is to stop the intake of phenacetin. One patient, who suffered from severe arthritis, refused steadfastly to abandon her codeine tablets without which she claimed life was intolerable. Although her son was a chemist, she would not accept any alternative analgesic, and her condition declined until she was lost to follow-up on leaving the district. Two other patients died within 2 months of the condition being diagnosed. Surprisingly, the remaining patients appeared to have no difficulty in abandoning a habit of many years' duration, and in each case renal function then slowly improved or in one case remained unchanged, while their general health also progressed favourably. Bell et al. (1969) showed that after withdrawal of the analgesic, renal function usually improves or remains stable, and only occasionally shows a slow decline. Our experience matches this. Urinary infection requires treatment by long term antibiotics. One of our patients (*Case* 2) showed steady improvement in her general condition and renal function following the withdrawal of the analgesic, the blood urea steadily falling to normal, but she became hypertensive and, in spite of prolonged therapy, urinary infection was never eradicated.

Surgical treatment

Separated papillae, especially if calcified, may cause blockage of the ureters and exacerbation of infection in pyramidal necrosis, whether caused by analgesic abuse or by diabetes. Hendry et al. (1972) described how these fragments, together with pus and debris, may be removed by a pyelotomy, and at the same time fragments lying in the ureter can be milked up or withdrawn using a Fogarty catheter. Fragments obstructing the lower ureter may be extracted with a stone basket (Hellebusch, 1969). We have not had occasion to employ these surgical measures, which are particularly indicated in the more acute type of pyramidal necrosis found in diabetes. In operating on cases of analgesic nephropathy, the experience of Koutsaimanis and de Wardener (1970) should be borne in mind. They reported that operations on patients with analgesic nephropathy carried a high mortality due to rapid deterioration of renal function. These patients are very susceptible to fluid loss, and preoperative dehydration, aggravated by hypotension and sodium loss, may reduce the medullary blood flow and compromise the vitality of the remaining papillae. Special attention must be paid to maintaining adequate hydration if operative treatment has to be carried out.

Analgesic abuse in other urological patients

In addition to the 9 patients discussed above, 24 patients were seen in the Urological Department who admitted taking excessive quantities of analgesics. We have arbitrarily defined analgesic abuse as an average dose of 10 tablets of codeine (or equivalent) per week, taken regularly for a minimum period of 2 years, but have relaxed this criterion to include 2 patients taking rather smaller doses for a much longer period of time and 1 patient who imbibed an enormous dose (140 codeine tablets weekly) for 9 months only. These patients had a similar sex and age distribution to those who were found to have fully developed analgesic nephropathy. Twenty of the 24 (83 per cent) were female and their ages varied from 20 to 67 with an average age of 41 years. Excessive analgesics were taken for periods varying from 9 months to 28 years with a mean of 8 years. In 6 cases the drugs were taken for the relief of arthritis or rheumatic conditions, but the remainder gave as their reasons either headache or 'migraine'. The analgesics favoured by the patients were mixtures containing phenacetin but, exceptionally, 2 patients took aspirin only. In 19 instances the intravenous pyelograms were normal. One patient had a stone in the right renal pelvis without evidence of pyramidal destruction. In 4 patients there was evidence of chronic pyelonephritis shown by clubbing of the calices and shrinkage of renal tissue. This group of 4 cases is important, as it may well include examples of analgesic nephropathy. The possibility of pre-existing pyelonephritis cannot be excluded, but analgesic abuse as a prime cause of the renal changes is suggested by the fact that 3 out of the 4 had abandoned analgesics a few years before they were seen by us. The pyelographic appearances may therefore represent a healing phase in the disorder. Reduced creatinine clearances indicated depressed renal function in 3 of the patients, 1 of whom was hypertensive. Of the 19 patients with normal intravenous pyelograms, 4 were hypertensive and 2 others had reduced creatinine clearances, but it is not possible to relate these findings firmly to their abuse of analgesics. None the less, in all these cases the renal tract is at risk, and all were urged to abandon the habit.

Discussion

Analgesic nephropathy is easily overlooked. Koutsaimanis and de Wardener (1970) estimated that there could be 500 new cases in England and Wales per annum, but by 1970 only 44 cases had been reported in the literature. It is imperative that all patients attending hospital with urinary symptoms should be questioned about analgesic intake. Any ambiguity in the reply should lead to closer interrogation, and the frequent concealment of the habit and underestimation of the dose should be remembered. The possibility of analgesic abuse should be borne in mind in cases of renal failure of unknown origin, in progressive chronic pyelonephritis and in patients with renal calculi or presenting with renal colic. Sterile pyuria may be a useful lead, and discovery of renal calculi with radiotranslucent centres should at once arouse the surgeon's suspicion. As mentioned above, we have records of 24 patients with excessive intake of analgesic associated with urinary symptoms but in whom we were unable to obtain radiological evidence of destruction of renal tissue. It is important that this group of patients should be identified, as the disease may be prevented by inducing the patients to abandon their addiction. In this way, not only may renal involvement be averted, but the patient may be spared the risk of developing carcinoma of the renal pelvis (Angervall et al., 1969). There is reason to believe, however, that analgesic nephropathy is a disease which will soon decline in frequency. Not only is the medical profession now familiar with the disorder, but presentations on television and other media have alerted the general public to the dangers of analgesic abuse. Some manufacturers have withdrawn phenacetin from their analgesic mixtures. The Department of Health and Social Security has restricted the sale of phenacetin-containing compounds to pharmacies only from 1 June 1974, and from 1 January 1975 phenacetin has been available only on a doctor's or dentist's prescription.

Although the finger of suspicion points most clearly to phenacetin as the responsible drug, it is still uncertain whether it is the only analgesic capable of inducing pyramidal necrosis, despite much clinical and animal research. We will not enter into details of this difficult problem, but until the matter is elucidated the clinician would be wise to regard both phenacetin and aspirin as culpable. Paracetamol, once regarded as innocent, has been implicated as a cause of analgesic nephropathy (Krikler, 1967), which is not surprising since paracetamol is a metabolic derivative of phenacetin. We have studied one case, not included in this series, in which pyramidal necrosis followed ingestion of paracetamol alone.

Acknowledgements

Our thanks are due to Mr M. Norton for the photographs and to Miss Anita Jones and Mrs J. Jenson for secretarial help.

References

ANGERVALL L., BENGTSSON U., ZETTERLUND C. G. and ZSIGMOND M. (1969) Renal pelvis carcinoma in a Swedish district with abuse of a phenacetin-containing drug. *Br. J. Urol.* **41**, 401–405.

BELL D., KERR D. N. S., SWINNEY J. and KEITH YEATES W. (1966) Analgesic nephropathy: clinical course after withdrawal of phenacetin. *Br. Med. J.* **3**, 378–382.

DAWBORN J. K., FAIRLEY K. F., KINCAID-SMITH P. and KING W. E. (1966) The association of peptic ulceration, chronic renal disease and analgesic abuse. *Q. J. Med.* **35**, 69–83.

VON FRIEDREICH N. (1877) Ueber Necrose der Nierenpapillen bei Hydronephrose. *Arch. Path. Anat. Phys. Klin. Med.* **69**, 308–312.

GAULT M. H., RUDWAL T. C., ENGLES W. D. and DOSSETOR J. B. (1968) Syndrome associated with the abuse of analgesics. *Ann. Intern. Med.* **68**, 906–925.

HELLEBUSCH A. A. (1969) Renal papillary necrosis. *JAMA* **210**, 1098–1100.

HENDRY W. F., HARRISON A. R. and KILPATRICK F. R. (1972) Surgical management of renal papillary necrosis. *Proc. R. Soc. Med.* **65**, 1023–1026.

KOUTSAIMANIS K. G. and DE WARDENER H. E. (1970) Phenacetin nephropathy with particular reference to the effects of surgery. *Br. Med. J.* **4**, 131–134.

KRIKLER D. M. (1967) Paracetamol and the kidney. *Br. Med. J.* **2**, 615.

LINDVALL N. (1960) Renal papillary necrosis: a roentgenographic study of 155 cases. *Acta Radiol.* **192**, Suppl., 153.

MURRAY R. M., TIMBURY G. C. and LINTON A. L. (1970) Analgesic abuse in psychiatric patients. *Lancet* **1**, 1303–1305.

NORDENFELT O. and RINGERTZ N. (1961) Phenacetin takers dead with renal failure. *Acta Med. Scand.* **170**, 385–402.

PRESCOTT L. F. (1966) Analgesic abuse and renal disease in North-East Scotland. *Lancet* **2**, 1143–1145.

SPÜHLER O. and ZOLLINGER H. U. (1953) Die chronisch-interstitielle Nephritis. *Z. Klin. Med.* **151**, 1–50.

DE WARDENER H. E. (1973) *The Kidney*, 4th ed. Edinburgh, Churchill Livingstone, pp. 322–325.

Br. J. Surg. Vol. 62 (1975) 303–304

The Fowler–Weir approach to appendicectomy

A. R. ASKEW*

SUMMARY

The medial approach of Fowler–Weir enables rapid opening of the abdominal cavity and provides good access to the appendix. Although there is less muscle trauma the wound seems as painful postoperatively as with the classic muscle-splitting approach. However, morbidity is less as shown by a decrease in the wound and deep infection rate compared with that after appendicectomy by the McBurney approach.

APPENDICECTOMY is the commonest abdominal surgical emergency, and since McBurney's classic description of appendicectomy in 1894 there have been numerous accounts of modifications, especially of the skin incision. Apart from the now obsolete Battle approach, the major modification to the approach to appendicectomy was published independently by George Fowler and Robert Weir in 1900. The Fowler–Weir approach has been evaluated in a series of 54 cases and compared with the classic muscle-splitting approach performed in a further 56 cases.

Materials and methods

One hundred and ten consecutive patients undergoing appendicectomy over a 10-month period were evaluated. Fifty-four patients were operated on by the Fowler–Weir (medial) approach and 56 by the standard right iliac fossa muscle-splitting approach. *Table I* summarizes the patients.

The indications for drainage of the wound and peritoneal cavity were standardized, as was the wound closure. An antibiotic spray (Framyspray) was sprayed into the wound in all cases. Postoperatively the number of analgesic injections required in each case was noted. The development of wound infection or deep abscesses was recorded.

In the Fowler–Weir approach the abdomen is opened by a skin incision overlying the lateral border of the right rectus abdominis muscle at or below the level of the anterior superior illiac spine (*Fig.* 1). The external oblique aponeurosis is then incised in the line of its fibres and the incision is extended horizontally across the anterior rectus sheath (*Fig.* 2). Medial retraction of the rectus muscle and the inferior epigastric vessels allows good exposure of the transversalis fascia and peritoneum which is then easily picked up and incised (*Fig.* 3). Closure of the wound is in layers with catgut, silk sutures being used for the skin.

Results

a. Non-perforated group

Forty-six patients in the Fowler–Weir group had non-perforated organs removed compared with 47 patients in the muscle-splitting group. Ten non-inflamed appendices were removed (9 per cent overall); 4 in the first group and 6 in the second.

In the Fowler–Weir group there were 4 cases of wound infection and 5 cases in the McBurney group. One patient in the former group developed a pelvic abscess.

Postoperative pain is difficult to assess but in the second to fourth decades when the condition is most common there was no great difference in the requirements of intramuscular analgesics of patients with non-perforated organs (*Table II*).

Table I: DETAILS OF THE PRESENT SERIES

	Fowler–Weir approach	McBurney approach
Total no.	54	56
Male	25	31
Female	29	25
Non-perforated	46	47
Perforated	8	9
Overall infection		
Wound	6 (11%)	9 (14%)
Deep	2 (3·7%)	3 (5·4%)

Table II: ANALGESIA REQUIREMENTS IN THE NON-PERFORATED GROUP

	Fowler–Weir approach		McBurney approach	
Age (yr)	No. of patients	Average no. of injections	No. of patients	Average no. of injections
10–19	21	1·7	17	1·8
20–29	10	2·6	17	2·6
30–39	5	2·4	4	2·9

b. Perforated group

Seventeen patients with perforated organs were seen, 8 having appendicectomy by the Fowler–Weir approach. Of these, 2 patients developed a wound abscess and 1 a pelvic abscess. Of the 9 patients having a routine appendicectomy, 3 developed pelvic collections and 4 developed wound infections. Again there was no obvious difference in the analgesia requirements of the two groups.

Overall there were 6 cases of wound infection in the Fowler–Weir group (11 per cent) and 8 in the McBurney group (14 per cent). The incidence of deep infection was 3·7 per cent in the former group and 5·4 per cent in the latter.

Discussion

The McBurney approach to appendicectomy is probably the commonest method in use today. His original description in 1894 describes the muscle-splitting

---

* Radcliffe Infirmary, Oxford.

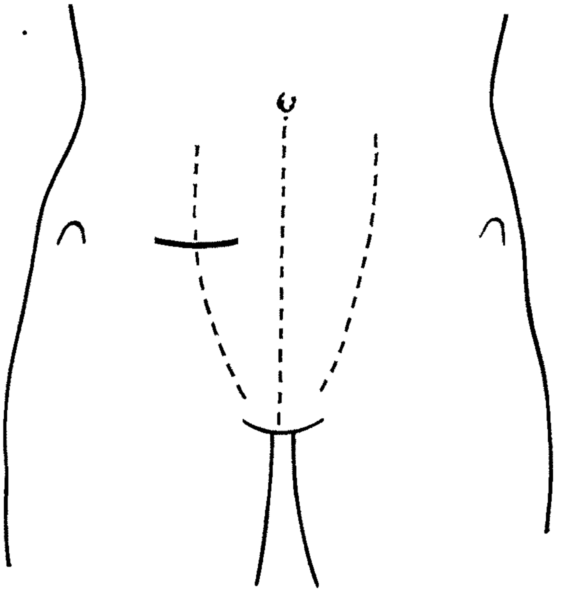


Fig. 1. Skin incision overlying lateral edge of rectus abdominis.

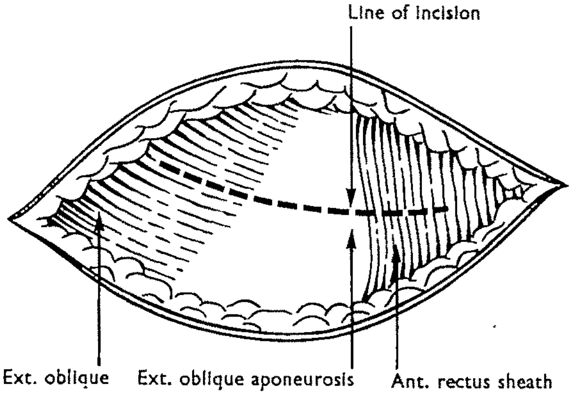


Fig. 2. Incision of external oblique aponeurosis and anterior rectus sheath.

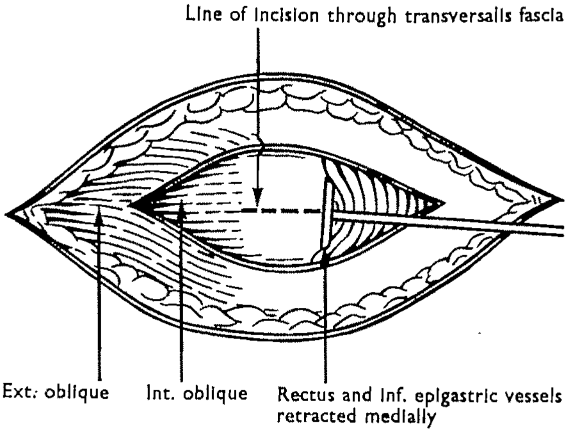

Line of Incision through transversalis fascia
Ext. oblique
Int. oblique
Rectus and Inf. epigastric vessels retracted medially

Fig. 3. Retraction of the rectus muscle and inferior epigastric vessels to expose the transversalis fascia which is incised.

technique following incision of the external oblique aponeurosis. The skin incision is made at right angles to a line joining the anterior superior iliac spine to the umbilicus, its upper one-third lying above the now famous McBurney's point. It is perhaps the skin incision which has undergone the most modification, and the skin crease incision of Lanz (1908) is now generally used.

In 1900 Fowler described his method of appendicectomy, but utilized an inverted L-shaped incision. He recommended his method for use in early cases and for 'interval' appendicectomy. Weir (1900) used the same approach for cases of acute appendicitis but did not describe the skin incision used.

The medial approach gives rapid access to the abdominal cavity and the access obtained is at least as good as that obtained by the classic approach. On 3 occasions further access was easily obtained by separation of the fibres of the internal oblique muscle in the lateral part of the wound, and this presents no greater difficulty than if extension is required with a classic approach. The approach presents little difficulty in obese patients, and the ovary is readily accessible providing there is good muscle relaxation.

The rapidity with which the abdomen can be opened and the minimal amount of muscle trauma are definite advantages in patients who are poor anaesthetic risks or who are on anticoagulant therapy. Jelenko and Davis (1973) recommended this approach for the latter group of patients. There is less muscle trauma with the medial approach, but this is not reflected postoperatively as assessed by the intramuscular analgesia requirements.

A theoretical objection is the opening of another tissue plane in an operation which has a high incidence of postoperative wound infection, but this has not been a problem in practice.

Although, surprisingly, the medial approach seemed no less painful in the postoperative period, the minimal muscle derangement may be an important factor in the subsequent development of wound infection. This is especially important in the perforated case, and in this group the incidence of wound infection was halved using the Fowler–Weir approach.

References

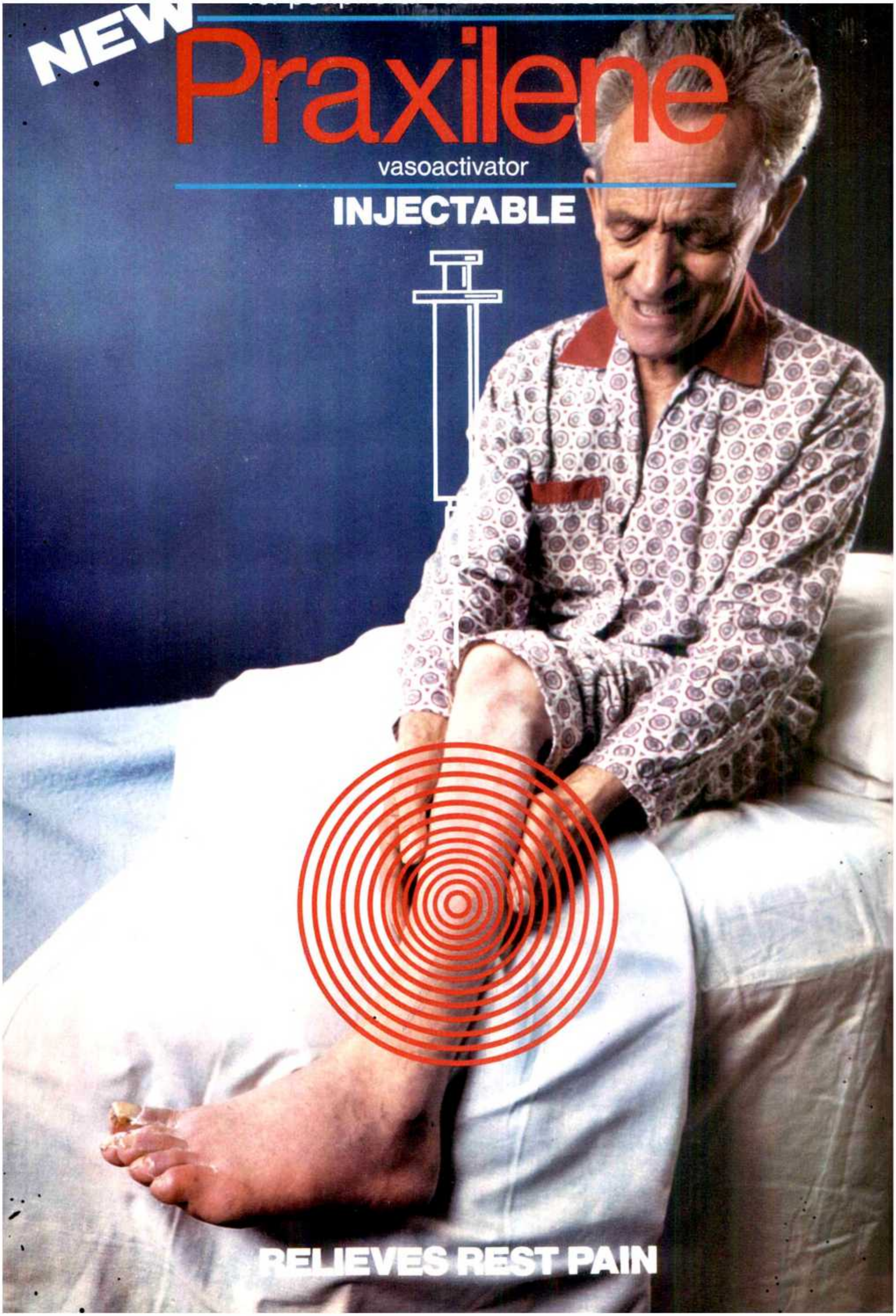
FOWLER G. R. (1900) A new and improved method of entering the abdominal cavity in the ileocaecal region. *Med. News* **76**, 321–324.

JELENKO C. and DAVIS L. P. (1973) A transverse lower abdominal appendicectomy incision with minimal muscle derangement. *Surg. Gynecol. Obstet.* **136**, 451–452.

LANZ O. (1908) Der McBurneyschen Punkt. *Zentralbl. Chir.* **35**, 185–190.

MCBURNEY C. (1894) The incision made in the abdominal wall in cases of appendicitis. *Ann. Surg.* **20**, 38–43.

WEIR R. F. (1900) An improved operation for acute appendicitis or for quiescent cases with complications. *Med. News* **76**, 241–242.


NEW
Praxilene
vasoactivator
INJECTABLE
RELIEVES REST PAIN

for peripheral vascular disorders

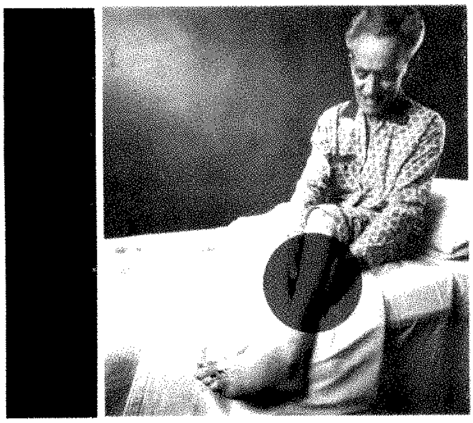
NEW Praxilene

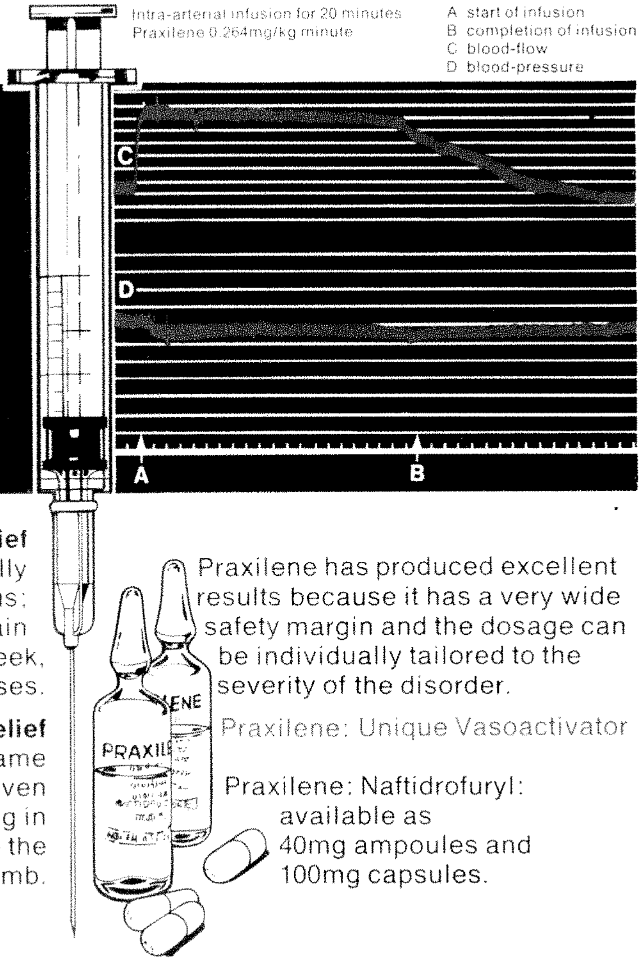
vasoactivator

INJECTABLE

RELIEVES REST PAIN

by flushing out pain producing metabolites
by improving blood-flow – without affecting blood-pressure
by a unique metabolic activity





Fast relief
Praxilene administered parenterally (Intra-arterial; Intravenous; Intramuscular) can give relief of pain within as short a time as one week, in many cases.

Prolonged relief
Relief of pain is prolonged: at the same time the collateral circulation is given the opportunity to develop, resulting in an improved blood supply to the affected limb.

Praxilene has produced excellent results because it has a very wide safety margin and the dosage can be individually tailored to the severity of the disorder.

Praxilene: Unique Vasoactivator

Praxilene: Naftidrofuryl:
available as
40mg ampoules and
100mg capsules.

Full prescribing information and dosage
schedule on request

Lipha (UK)
West Drayton, Middlesex
Telephone: West Drayton 49331/2

Br. J. Surg. Vol. 62 (1975) 305–308

Subphrenic abscess in children

M. MACKENZIE, J. FORDYCE AND D. G. YOUNG*

SUMMARY

Nineteen consecutive cases of subphrenic abscess which were treated in the Royal Hospital for Sick Children, Glasgow, from 1962 to 1972 are analysed. This complication of intra-abdominal suppuration of surgery still carries a grave prognosis. Four of the patients died (21 per cent); 2 deaths were related to the subphrenic abscess while the remaining 2 were not directly related to the abscess. The mean hospital stay of the survivors was 59 days (range 30–122 days). The changing patterns of aetiology and presentation which have recently been emphasized in general surgical practice are not reflected in this paediatric series.

SUBPHRENIC abscess is a serious complication of intra-abdominal sepsis or surgery. Before the era of surgery and antibiotics this disease was usually fatal, with a mortality reported as 47·4 per cent (Barnard, 1908) and 50 per cent (Piquand, 1909). Despite surgical technical advances, Oschner and DeBakey (1938) reported a mortality of 32·8 per cent in operated cases and 89·9 per cent in non-operated cases. Since the introduction of antibiotic therapy the mortality rate has been reported as low as 7·5 per cent (Ozeran, 1967), but in most series it remains higher between 14 and 35 per cent with surgery, and 30–94 per cent without surgery (Wetterfors, 1959; Dineen and McSherry, 1962; Carter and Brewer, 1964; Magilligan, 1968; Sherman and Davis, 1969; Halasz, 1970; Konvolinka and Olearczyk, 1972).

Contemporary adult surgical experience shows subphrenic abscess to be a postoperative complication of surgery for a non-inflammatory condition or for a perforated peptic ulcer (Sanders, 1970a; Surakiatchanukul and Ram, 1973). In paediatric surgical practice the commonest cause is still the intra-abdominal infection of appendicitis or primary peritonitis where early surgery does not always avert a subphrenic collection. The clinical pattern in children is usually that of an acute secondary illness occurring soon after surgery for primary inflammatory disease. With widespread use of antibiotics the presentation is often insiduous (Moller, 1967; Sanders, 1970a), and this may cause delay in instituting specific therapy.

This review is of recent experience with subphrenic abscess in the paediatric age group. It has been made to determine the present aetiology, morbidity and mortality of this condition.

Patients

This study was based on 19 consecutive cases of proved subphrenic abscess treated at the Royal Hospital for Sick Children, Glasgow, in the 11 years from 1962 to 1972. Four patients had bilateral subphrenic abscesses, i.e. the total number of abscesses was 23. The mean age of the patients was 5 years 7 months, the youngest being an infant of 8 months and the oldest a 12-year-old girl. Ten of the patients were male. The length of time spent in hospital varied from 30 to 122 days.

During this 11-year period there was an average of 210 patients (range 160–253) admitted each year with clinical and histologically confirmed acute appendicitis. Subphrenic abscess occurred in 8 of these patients, i.e. an incidence of 0·35 per cent. In addition, a further 3 children were admitted with an established appendix abscess, but appendicectomy was only performed later as an 'interval' procedure. If patients with appendicitis and its complications are considered separately, then the incidence of subphrenic abscess is 0·45 per cent.

Table I: CLINICAL PRESENTATION AND SIGNS IN 19 PATIENTS WITH SUBPHRENIC ABSCESS

Sign or symptom	No. of cases
Pyrexia, temperature elevation >37·5 °C	17
Leucocytosis (>10 000/mm^3)	15
Abdominal pain	15
Abdominal swelling and tenderness	12
Haemoglobin < 10 g/100 ml	11
Basal atelectasis	11
Elevation of hemidiaphragm	11
Pleural effusion	6
Gas under diaphragm	6

Presentation

The common signs and symptoms of the 19 patients are presented in *Table I*. Pyrexia above 37·5 °C which had either failed to settle or having settled began to fluctuate was present in 17 patients. Temperatures ranged up to 39·5 °C. The general condition of the children varied from a child with general malaise to that of the severely ill and toxic patient. Abdominal pain was present in 15 patients, and in 12 there was abdominal distension and marked abdominal tenderness. Shoulder tip pain was not a prominent feature. In the younger patients this may have been attributed to poor localization of pain, but it was also uncommon in the older children. An increased respiratory rate and an unproductive cough were common symptoms. Leucocytosis with predominantly a polymorphonuclear increase ranging from 10 000 to 23 000/mm^3 was present in 15 patients.

The diagnosis was usually made on clincial grounds with supporting evidence from radiological investigation. Gas under the diaphragm was present in only 6 patients. Basal atelectasis, elevation of the diaphragm and pleural effusion were the commonest radiological signs and were present in 11 patients. When screening was performed limitation of movement of the hemidiaphragm on the side of the abscess was observed in every patient. Complete immobility of the diaphragm is probably a late manifestation of the condition since movement was retained with a subhepatic abscess better than with a suprahepatic abscess.

---

* Royal Hospital for Sick Children, Yorkhill, Glasgow.

Aetiology

The primary condition preceding subphrenic abscess is shown in *Table II.* Acute appendicitis was the primary disease in 11 patients, with primary Gram-positive peritonitis causing 4 of the remaining subphrenic abscesses. The 2 patients with abscesses resulting from elective surgery followed splenectomy for portal hypertension and an interval appendicectomy. The pelvic abscess was of unknown aetiology, no visceral abnormality being found at laparotomy. The patient with ulcerative colitis was a 9-year-old girl who had a 3-week history of the disease. She had emergency colectomy following perforation of the colon. A left subphrenic abscess was drained 2 days later.

Appendicitis

Eight of the patients with acute appendicitis were operated on within 12 hours of admission and each was noted to have a macroscopic perforation of the appendix. The peritoneal cavity was drained in all of these patients but they proceeded to develop a subphrenic abscess. One patient admitted 6 days after the onset of symptoms had a pelvic abscess drained initially but it was felt that the appendix could not be safely removed at that time. The other 2 patients had an apparently localized right iliac fossa mass on admission and were treated conservatively. Subsequently each developed signs of a subphrenic abscess which necessitated surgical intervention. Following discharge these 3 patients returned for interval appendicectomy, and in 1, closure of a faecal fistula from the caecum.

Table II: PRIMARY CONDITION PRECEDING DEVELOPMENT OF SUBPHRENIC ABSCESS

Primary condition	No. of cases	%
Acute appendicitis	11	57·9
Primary peritonitis	4	21·0
Postsurgical	2	10·5
Ulcerative colitis	1	5·3
Pelvic abscess	1	5·3

Primary peritonitis

The causative organisms of the Gram-positive peritonitis which was complicated by subphrenic abscess were *Staphylococcus aureus* in 3 patients and pneumococcus in 1. Two of these patients had early laparotomy as a definitive diagnosis had not been made. One patient, an 8-month-old infant suffering from staphylococcal peritonitis, was known to have chronic granulomatous disease, and one girl was subsequently extensively investigated for evidence of granulomatous disease but with negative results. Three of these patients had been generally well prior to and since their intraperitoneal infection. Two gave a history of recent throat infection and one had just recovered from measles when the abdominal signs developed.

Bacteriology

Table III presents the bacteria cultured from the pus in the subphrenic space. In 2 patients no organisms were cultured from the subphrenic pus. Each of these patients had been treated with ampicillin and ceporin and these drugs may have eliminated the causal organisms. Gram-negative organisms predominated, and with the exception of the primary peritonitis patients all the organisms cultured were in this group.

Table III: ORGANISMS CULTURED FROM PUS IN SUBPHRENIC ABSCESS AND PRECEDING ANTIBIOTIC THERAPY

	Organism isolated							
Abscess aetiology	*E. coli*	*Str. faecalis*	*Bacteroides* sp.	*Klebsiella* sp.	*Haemophilus* sp.	*Staph. aureus*	*Pneumococcus* sp.	Antibiotics used
Appendicitis	+		+					Ceporin, ampicillin
Appendicitis	+		+					Ceporin, ampicillin
Appendicitis	+	+		+				Ceporin, ampicillin
Appendicitis	+	+						Ampicillin
Appendicitis	+	+						Ampicillin
Appendicitis	+		+		+			Ampicillin
Appendicitis	+		+					Septrin
Appendicitis		+		+				Tetracycline
Appendicitis	NG							Ceporin, ampicillin
Appendicitis	NG							Ceporin, ampicillin
Appendix abscess			+					Gentamicin, ceporin
Primary peritonitis						+		Cloxacillin, ampicillin
Primary peritonitis						+		Cloxacillin, ampicillin
Primary peritonitis						+		Cloxacillin
Primary peritonitis							+	Ampicillin
Postoperative	+							None
Postoperative	+							None
Pelvic abscess	+							Ampicillin
Ulcerative colitis	+	+						Ceporin

NG, No growth.

Treatment

The initial therapy was usually for the primary inflammatory process, and in 16 patients the initial surgery was combined with antibiotic therapy. Ampicillin and cerporin were the most commonly used antibiotics. The subphrenic abscess was diagnosed from 2 to 39 days after operation and was subsequently drained. Two patients with an appendix abscess were treated conservatively at first and a subphrenic abscess was suspected soon after admission. The subphrenic abscess was drained later when it was not resolving adequately on conservative therapy.

The site of the abscess has been classified in *Table IV*. In 4 children bilateral abscesses were present and these were suprahepatic. Subphrenic abscesses are primarily intraperitoneal, and in 14 patients drainage of the abscess was by direct approach without crossing uncontaminated peritoneal cavity. In the 4 bilateral cases an epigastric transperitoneal approach was made to the abscesses.

The drainage route is shown in *Table IV*. Six patients developed a pleural effusion but only 1 patient developed a purulent collection in the pleural cavity, and at autopsy on this child micro-abscesses were present in the lung. There were no other intrathoracic complications such as rupture of the diaphragm or bronchial fistula. In 3 patients drainage was inadequate and a second operation was necessary to drain the abscess. In addition to the administration of antibiotics, adequate fluid, electrolyte and blood, when necessary, therapy was supplemented by intravenous feeding. High calorie intake may be necessary for some time, e.g. a calorie intake of 140 Cal/kg body weight for 2–3 months in one child. This child had a klebsiella septicaemia and subsequently a candida septicaemia, at which time all antibiotic therapy was discontinued and antifungal therapy given. With continuing intravenous nutrition he slowly responded. When septicaemic this patient also required mechanical ventilation for 6 days until adequate spontaneous ventilation could be maintained again.

Mortality

Four patients died in this series. One of these was the infant with chronic granulomatous disease in whom the subphrenic abscess was a further complication of his primary disease. The child with ulcerative colitis also died on the morning following operation for drainage of the abscess. One patient of 21 months had acute necrotizing appendicitis in a subhepatic appendix associated with incomplete rotation of the gut. He died 32 days later with evidence of intraperitoneal, intrahepatic and pulmonary infection continuing. The remaining child with appendicitis died 17 days after admission and 9 hours after drainage of 600 ml of pus from a right subphrenic abscess.

Discussion

Subphrenic abscess in children has not shown the change in aetiology which has been reported in adults (Moller, 1967; Rosenberg, 1968; Sanders, 1970a). The present series corresponds more to the aetiology of subphrenic abscess in general surgery reported prior to 1940 (Barnard, 1908; Fifield and Love, 1926; Oschner, 1931; Oschner and DeBakey, 1938). The reasons for this are not altogether clear. Appendicitis continues to be the main predisposing factor, and delay in diagnosis of acute appendicitis still continues in children.

Table IV: SITE OF ABSCESS AND DRAINAGE APPROACH

Position	No. of cases	Drainage approach
Right suprahepatic	12	Anterior subcostal
Right infrahepatic	1	Posterior
Left suprahepatic	2	Anterior subcostal
Left infrahepatic	0	—
Bilateral	4	Epigastric

Subphrenic abscess was reported by Delario (1934) to be a complication in 0·9 per cent of patients with acute appendicitis, while earlier in this century Newhof (1912) reported the incidence as 1·5 per cent. More recently, Moller (1967) and Sanders (1970b) have reported the incidence of subphrenic abscess complicating appendicitis as 0·3 and 0·4 per cent respectively. This is in parallel with the Glasgow experience of 0·35 per cent when only histologically confirmed acute appendicitis is considered, and 0·45 per cent when in addition patients with clinically diagnosed appendix abscess are included.

In this series primary peritonitis preceded subphrenic abscess in 21 per cent of the patients. Primary peritonitis has been reported as a complication of Gram-positive bacteriaemia in children (Harken and Shockat, 1973). In the present series there were 3 staphylococcal abscesses and in only one of these children was a predisposing cause found. The suspected increase in primary peritonitis in patients with the nephrotic syndrome or those on steroid or immunosuppressive therapy has not yet resulted in intraperitoneal infection and subsequent subphrenic abscess.

The mortality in the present series remains high at 21 per cent. One infant died primarily from his chronic granulomatous disease. Repetition of the remaining 3 deaths may now be avoidable with the current armamentarium of antibiotics, intravenous fluids and feeding, assisted ventilation and intensive monitoring.

Direct treatment of the abscess remains along the basic lines of standard surgical practice. Once diagnosed a brief period of intensive antibiotics and resuscitative treatment may be beneficial to produce optimal conditions for drainage. The antibiotic to be used in each patient will depend on the primary condition, as in the appendicitis patient a Gram-negative infection is very likely, while in primary peritonitis a Gram-positive organism is probable. Ampicillin was the most commonly used antibiotic in this series, but with gradual changes in the pattern of coliform sensitivity it is less valuable and a cephalosporin or gentamicin may be preferred. Estimation of the serum level of the antibiotic is important in the severely ill patient to ensure that adequate blood levels are obtained but toxic levels are avoided.

Twenty-five years ago with the emergence of antibiotics it must have seemed that subphrenic abscess would be a subject on which the younger generation would have no experience. However, the present series indicates that subphrenic abscess remains a problem causing mortality and morbidity in the younger age group. The most effective action to decrease this problem further is for prompt diagnosis of acute appendicitis to be made in children and appropriate therapy instituted.

Acknowledgements

We wish to thank the surgeons at the Royal Hospital for Sick Children, Glasgow, for permission to review patients admitted under their care.

References

BARNARD H. L. (1908) Surgical aspects of subphrenic abscess. *Br. Med. J.* **1**, 371–377.

CARTER R. N. and BREWER L. A. (1964) Subphrenic abscess: a thoraco-abdominal clinical complex. *Am. J. Surg.* **108**, 165–174.

DELARIO A. J. (1934) Subdiaphragmatic abscess. *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **31**, 177–190.

DINEEN P. and MCSHERRY C. K. (1962) Subdiaphragmatic abscess. *Ann. Surg.* **155**, 506–517.

FIFIELD C. R. and LOVE R. J. M. (1926) Subphrenic abscess. *Br. J. Surg.* **13**, 683–695.

HALASZ N. A. (1970) Subphrenic abscess: myths and facts. *JAMA* **214**, 724–726.

HALLIDAY P. and LOEWENTHAL J. (1964) Subphrenic abscess. *Aust. NZ J. Surg.* **33**, 260–268.

HARKEN A. H. and SHOCKAT S. J. (1973) Gram-positive peritonitis in children. *Am. J. Surg.* **125**, 769–772.

KONVOLINKA C. W. and OLEARCZYK A. (1972) The subphrenic abscess. *Curr. Probl. Surg. Jan.* pp. 1–51.

MAGILLIGAN D. J. (1968) Suprahepatic abscess. *Arch. Surg.* **96**, 14–19.

MAINGOT R. (1970) *Abdominal Operations.* New York, Appleton-Century-Crofts, p. 800.

MOLLER C. (1967) Subphrenic abscess: a clinical study of 20 cases. *Acta Chir. Scand.* **133**, 153–156.

NEWHOF H. (1912) Non-suppurative peritonitis complicating appendicitis. *Surg. Gynecol. Obstet.* **14**, 231.

OSCHNER A. (1931) Subphrenic abscess: its diagnosis and treatment, with special reference to the extraperitoneal operation. *Int. Clin.* **2**, 79.

OSCHNER A. and DEBAKEY M. (1938) Subphrenic abscess. *Int. Abstr. Surg.* **66**, 426–433.

OZERAN R. S. (1967) Subdiaphragmatic abscess: diagnosis and treatment. *Am. J. Surg.* **33**, 64–67.

PIQUAND G. (1909) Les abcès sous-phréniques. *Rev. Chir.* **39**, 156–179.

ROSENBERG M. T. (1968) Chronic subphrenic abscess. *Lancet* **2**, 379–380.

SANDERS R. C. (1970a) Changing epidemiology of subphrenic abscess and its clinical and radiological consequences. *Br. J. Surg.* **57**, 449–455.

SANDERS R. C. (1970b) Post-operative pleural effusion and subphrenic abscess. *Clin. Radiol.* **21**, 308–312.

SHERMAN N. J. and DAVIS J. R. (1969) Subphrenic abscess: a continuing hazard. *Am. J. Surg.* **117**, 117–123.

SURAKIATCHANUKUL S. and RAM M. D. (1973) Current patterns of subphrenic abscess. *Am. J. Surg.* **125**, 718–720.

WETTERFORS J. (1959) Subphrenic abscess: a clinical study of 101 cases. *Acta Chir. Scand.* **117**, 338–408.

Br. J. Surg. Vol. 62 (1975) 309–312

The cause and treatment of postvagotomy diarrhoea

JOHN R. CONDON, V. ROBINSON, M. I. SULEMAN, V. S. FAN
AND M. D. McKEOWN*

SUMMARY

Six patients with watery postvagotomy diarrhoea and 4 patients with intractable diabetic diarrhoea were treated with cholestyramine. The diarrhoea responded completely to therapy, during which the stool content of water, sodium, potassium and magnesium fell. Two of the patients, while receiving cholestyramine, had a rise in faecal fat, but this was not accompanied by diarrhoea, the stools being well formed.

Evidence is presented which suggests that the mechanism of diarrhoea is similar in both disorders and is due to division or neuropathy of the hepatic fibres of the vagus nerve. This results in distension of the gallbladder, contraction of which expels increased quantities of bile salts, which swamp the reabsorptive capacity of the small intestine and induce diarrhoea by direct action on the colon. If this theory is valid, cholecystectomy, by preventing large quantities of concentrated bile salts from suddenly entering the gut, may result in improvement of postvagotomy and diabetic diarrhoea.

VAGOTOMY accompanied by pyloroplasty or gastrojejunostomy is a frequently performed surgical procedure. It is sometimes complicated by diarrhoea which may respond to symptomatic medication or special attention to diet. Failure to respond to these simple measures indicates the presence of intractable diarrhoea, a most difficult long term management problem.

A series is reported of 6 postvagotomy patients and 4 diabetic patients with intractable diarrhoea which responded to cholestyramine, an anion exchange resin which binds bile salts in the gut. Our evidence suggests that the mechanism of diarrhoea is similar in both disorders, and a hypothesis is advanced to account for the change in bowel habit which may follow vagotomy.

Case reports

Case 1: A 58-year-old man had a truncal vagotomy and pyloroplasty in 1968 because of chronic duodenal ulceration. Division of the vagus was confirmed histologically and a postoperative insulin test showed no response to hypoglycaemia (blood sugar 21 mg/100 ml). Severe watery diarrhoea developed postoperatively but was controlled by codeine phosphate. However, the diarrhoea became progressively more severe and persistent, with 6–7 unformed stools daily, despite continuation of codeine therapy. Codeine phosphate was discontinued for 10 days before treatment with cholestyramine (4 g twice daily) was started. The diarrhoea stopped during cholestyramine administration but recurred when the compound was stopped; symptoms were recontrolled when therapy was restarted.

Case 2: A 57-year-old man had a partial gastrectomy in 1969 for a gastric ulcer. Eight months later he had a Heller operation for achalasia of the cardia, but 6 months postoperatively progressive dysphagia again developed. The stomach remnant and lower oesophagus were removed and a Roux-en-Y oesophagojejunostomy was performed. During this procedure a total vagotomy was carried out. Postoperatively the patient developed severe watery diarrhoea, 6–10 stools daily, there being little response of the diarrhoea to symptomatic treatment which was continued for 3 years. When cholestyramine (4 g thrice daily) was given the diarrhoea stopped, stools became well formed and their number fell to 1–2 per day.

Cases 3, 4, 5, and 6: Four subjects all had diarrhoea following vagotomy and pyloroplasty for chronic duodenal ulceration. The patients had 5–8 watery stools daily and there was poor response to symptomatic treatment in all the cases. Bowel habit and faecal appearance returned to normal in every patient when cholestyramine (4 g three times daily) was given. Diarrhoea recurred when cholestyramine was withdrawn but was recontrolled when the compound was restarted.

Case 7: A male aged 37 years had been a diabetic for 24 years. There had been evidence of peripheral neuropathy for 7 years and diabetic retinopathy for 5 years. Diarrhoea had been present for 16 years and was at first intermittent, lasting 3–5 days. The diarrhoea became progressively worse and at times there were 15–20 bowel actions per day, although 10 stools daily were the average. Investigations of the gastro-intestinal tract including three barium enema examinations were negative. There was no response to treatment with pancreatic extracts, codeine phosphate, antispasmodics, antibiotics, diphenoxylate and methylcellulose. Oral administration of cholestyramine (4 g thrice and later twice daily) resulted in a reduction of the frequency of stools to 1–2 daily, with 'solidification' of the faeces. Diarrhoea recurred when cholestyramine was withdrawn for two separate periods of time, but on both occasions the patient responded when cholestyramine was restarted.

Case 8: A 52-year-old man had suffered from diabetes mellitus for 25 years. There was marked evidence of peripheral neuropathy and diabetic retinopathy. Diarrhoea unresponsive to conventional therapy occurred 6–8 times daily. Cholestyramine (4 g twice daily) resulted in a reduction in bowel actions to once daily, the stools being well formed. Withdrawal of cholestyramine resulted in recurrence of diarrhoea until the drug was re-introduced.

Cases 9 and 10: Two diabetic subjects with evidence of peripheral neuropathy had had diarrhoea for 4 and 10 years respectively. There had been only limited control of diarrhoea with codeine phosphate. Cholestyramine (4 g once daily and later 4 g twice daily) reduced bowel movements to one per day.

Table I shows the faecal fat, sodium, potassium, magnesium and fluid contents of the stools in *Cases* 1, 2 and 3 when they were and were not treated with cholestyramine. In all the patients cholestyramine was suspended in water and drunk with the main meals.

Discussion

We have reported 6 postvagotomy and 4 diabetic subjects with intractable diarrhoea which responded to treatment with cholestyramine. Ayulo (1972) has also reported that patients with postvagotomy diarrhoea respond to oral cholestyramine therapy.

---

* St Mary's Hospital, Eastbourne.

Table I: STOOL CONSTITUENTS AND BOWEL HABIT IN 3 PATIENTS WITH POSTVAGOTOMY DIARRHOEA BEFORE AND AFTER TREATMENT

	Case 1			*Case* 2			*Case* 3		
	Before	After	Reduction (%)	Before	After	Reduction (%)	Before	After	Reduction (%)
Daily dosage of cholestyramine (g)	0	8	—	0	12	—	0	12	—
Daily stool frequency	6–7	1	84	6–10	1–2	80	7–8	1–2	75
Total stool weight (g)	1256	560	56	2277	843	63	1132	931	18
Dry stool weight (g)	150	143	5	121	177	46*	153	222	45*
Fluid content of stool (g)	1102	417	52	2156	666	69	979	709	28
Stool fat (g)	22	15	31	34·5	70·5	104*	29·2	66·0	126*
Stool sodium (mEq)	25	2	92	247	18	92	70	46	43
Stool potassium (mEq)	33	11	66	142	94	33	57	77	35*
Stool magnesium (mEq)	—	—	—	32	12	62	52	36	31

Stool constituents based on 5-day collection.
* Percentage increase.

Postvagotomy and diabetic diarrhoea have many clinical features in common; in both disorders bowel movements are frequent and defaecation may occur without warning, the faeces may be watery in consistency and there may be steatorrhoea, delayed gastric emptying and disordered transit through the small intestine (Wruble and Kalser, 1964).

Complete division of the vagi results in enlargement of the gallbladder, which almost doubles its fasting volume and contracts poorly (Johnson and Boyden, 1952; Rudick and Hutchison, 1964; Inberg and Vuorio, 1969). Likewise diabetics are known to have large volume, poorly contracting gallbladders (Gitelson et al., 1963). A high incidence of gallstones is found following vagotomy (Reynolds, 1962; Nielsen, 1964) and also in diabetic subjects (Lieber, 1952). Furthermore, in both disorders examination of the gut has failed to reveal pathological changes to account for the diarrhoea, which is particularly resistant to therapy.

The almost invariable association of diabetic diarrhoea with visceral and peripheral neuropathy is highly suggestive of a neuropathy involving the vagus nerve, so that the mechanism of diabetic diarrhoea may be similar to that of diarrhoea following vagotomy.

The incidence of diarrhoea following truncal vagotomy can be reduced from 25 per cent to only 2 per cent by selective vagotomy, when the coeliac and hepatic branches of the vagus nerve are preserved (Johnston et al., 1972). These vagal branches supply the biliary system and pancreas. A disturbance of pancreatic exocrine secretion resulting in diarrhoea is, however, unlikely as neither diabetic nor postvagotomy subjects with diarrhoea usually respond to therapy with pancreatic extracts.

The fact that our patients with postvagotomy and diabetic diarrhoea responded to cholestyramine (an anion exchange resin which binds with bile acids) strongly suggests that in these disorders excess quantities of bile are reaching the colon. Increased quantities of bile acids have, in fact, been demonstrated in the faeces in postvagotomy patients (Allan et al., 1973a; Gerskowitch et al., 1973), and when individual bile acids are measured there is a highly significant increase in the excretion of chenodeoxycholic acid (Allan et al., 1973b). Saburov (1961) has reported increased bile flow in experimental animals when hydrochloric acid was introduced into the duodenum following section of the vagus. Secretin and other hormones may be involved in the stimulation of bile flow demonstrated by Saburov (1961). There is, however, no general agreement as to the effect of vagotomy, since Baldwin et al. (1966) have demonstrated decreased bile flow following vagotomy. Bile salt concentration is increased following vagotomy (Smith et al., 1973), and although the gallbladder usually contracts within 30 minutes of eating, resulting in a sharp rise in duodenal bile salt concentration (Sjovall, 1959), the concentration of bile salts in the postprandial aspirate is low following vagotomy (Fields and Duthie, 1965).

These facts suggest that gallbladder contraction is not in phase with gastric emptying, thus resulting in poor admixture of bile and chyle. Not only may there be poor admixture of bile and chyle but if the overall volume of the gallbladder is approximately twice normal (even in the presence of a mild defect of emptying) increased quantities of bile would pass into the gut. A high concentration of bile salts entering the small gut at inappropriate times could swamp the reabsorptive capacity of the ileum and enter the colon, partly undergoing deconjugation and resulting in diarrhoea (Sobotka, 1937). The probable existence of a limited reabsorptive capacity of the small intestine for bile salts can easily be demonstrated by feeding pure bile salts, when after a few days, severe diarrhoea results (Hardison and Rosenberg, 1967; Hofmann, 1968). Indeed, if free and conjugated bile salts are perfused through the colon, there is inhibition of absorption of sodium chloride, potassium and water (Mekhjian et al., 1971) and disturbances of colonic activity (Galapeaux et al., 1938), all features contributing to the resultant diarrhoea. Wingate et al. (1973) have also shown that conjugated dihydroxy bile acids inhibit electrolyte and fluid absorption and at high concentration evoke secretion of isotonic fluid in the jejunum. It has been suggested that this also contributes to the diarrhoea induced by bile salts (Low-Beer, 1973).

The only diarrhoea of known aetiology which responds to cholestyramine is that which occurs following resection or disease of the terminal ileum (Hardison and Rosenberg, 1967; Van Deest et al., 1968), when there is malabsorption of bile salts which enter the colon in excess (Row, 1967; Stanley and Nemchausky, 1967; Meihoff and Kern, 1968). Chenodeoxycholic acid is thought to play a major role in diarrhoea due to ileal resection (Poley et al., 1972), and Allan et al. (1973a b,) showed that increased faecal concentrations of this bile acid occur in patients with postvagotomy diarrhoea. These findings, taken in conjunction with the fact that patients with diarrhoea due to ulcerative colitis and idiopathic tropical sprue fail to respond to cholestyramine therapy (McCloy and Hofmann, 1971; Miettinen, 1971; Condon, 1973), are highly suggestive that postvagotomy diarrhoea is due to excess quantities of bile salts entering the colon. Furthermore, oral administration of cholestyramine, by binding bile salts and thus preventing their effects on the gut, resulted in a marked fall in fluid contents of the stool in the present series (*Table I*). The fall in faecal fluid was associated with a decrease in faecal sodium, potassium and magnesium, except in *Case* 3, in whom stool potassium rose.

In 1 patient the faecal fat fell, whereas in 2 other subjects (*Cases* 2 and 3) steatorrhoea occurred during cholestyramine therapy. Cholestyramine is known to induce steatorrhoea by binding bile salts, and it is of interest that the 2 patients receiving 12 g of the resin daily developed steatorrhoea (though not diarrhoea), whereas the patient taking 8 g of cholestyramine daily had a fall in faecal fat. The optimum dose of cholestyramine should therefore control diarrhoea and result in a fall of faecal fluid, fat, sodium, potassium and magnesium. Further experience of the use of the resin in our patients suggests that a dose of 2 g of cholestyramine twice to four times per day controls diarrhoea without inducing steatorrhoea.

We therefore propose that intractable diarrhoea in postvagotomy and diabetic subjects is due to surgical resection or neuropathy of vagal fibres which control gallbladder function. Increased quantities of bile salts are released into the small intestine, swamping its reabsorptive capacity. Diarrhoea is induced by a direct action of bile acids on the colon. The effect of bile salts, which inhibit intestinal absorption of water and electrolytes, can be counteracted by treatment with cholestyramine. If this theory is correct, then cholecystectomy, by preventing large quantities of concentrated bile salts from suddenly entering the gut, may result in improvement of postvagotomy and diabetic diarrhoea.

Acknowledgement
V. Robinson was supported by a research grant from the South East Metropolitan Regional Hospital Board.

References

ALLAN J. G., GERSKOWITCH V. P. and RUSSELL R. I. (1973a) A study of the role of bile acids in the pathogenesis of post vagotomy diarrhoea. *Gut* **14**, 423–424.

ALLAN J. G., GERSKOWITCH V. P., and RUSSELL R. I. (1973b) Bile acids and post vagotomy diarrhoea. *Br. Med. J.* 4, 741.

AYULO J. A. (1972) Cholestyramine in post vagotomy syndrome. *Am. J. Gastroenterol.* **57**, 207–226.

BALDWIN J., HEER W. F., ALBO R., PELOSO O., RUBY L. and SILEM W. (1966) The effect of vagus nerve stimulation on hepatic secretion of bile in human subjects. *Am. J. Surg.* **111**, 66–69.

CONDON J. R. (1973) Personal observation.

FIELDS M. and DUTHIE H. L. (1965) Effect of vagotomy on intraluminal digestion of fat in man. *Gut* **6**, 301–310.

GALAPEAUX E. A., TEMPLETON E. D. and BORKON E. L. (1938) The influence of bile on the motility of the dog's colon. *J. Physiol.* **121**, 130–136.

GERSKOWITCH V. P., ALLAN J. G. and RUSSELL R. I. (1973) Increased secretion of bile acids in post-vagotomy diarrhoea. *Br. J. Surg.* **60**, 912.

GITELSON S., SCHWARTS A., FRAENKEL M. and CHOWERS I. (1963) Gall bladder dysfunction in diabetes mellitus. The diabetic neurogenic gall bladder. *Diabetes* **12**, 308–312.

HARDISON W. G. M. and ROSENBERG I. H. (1967) Bile salt deficiency in steatorrhoea following resection of the ileum and proximal colon. *New Engl. J. Med.* **277**, 337–342.

HOFFMAN A. F. (1968) Function of bile in the alimentary canal. In: CODE C. F. (ed.) *Handbook of Physiology*, sect. 6, vol. 5. Washington, American Physiology Society, pp. 2507–2533.

INBERG M. V. and VUORIO M. (1969) Human gall bladder function after selective gastric and total abdominal vagotomy. *Acta Chir. Scand.* **135**, 625–633.

JOHNSON F. E. and BOYDEN E. A. (1952) The effect of double vagotomy on the motor activity of the human gall bladder. *Surgery* **32**, 591–601.

JOHNSTON D., HUMPHREY C. S., WALKER B. E., PULVERTAFT C. N. and GOLIGHER J. C. (1972) Vagotomy without diarrhoea. *Br. Med. J.* 3, 788–790.

LIEBER M. M. (1952) The incidence of gall stones and their correlation with other diseases. *Ann. Surg.* **135**, 394–405.

LOW-BEER T. S. (1973) Diabetic diarrhoea. *Br. Med. J.* 4, 741.

MCCLOY R. M. and HOFMANN A. F. (1971) Tropical diarrhoea in Vietnam—a controlled study of cholestyramine therapy. *New Engl. J. Med.* **284**, 139–140.

MEIHOFF W. E. and KERN F. (1968) Bile salt malabsorption in regional ileitis, ileal resection and mannitol induced diarrhoea. *J. Clin. Invest.* **47**, 261–267.

MEKHJIAN H. S., PHILLIPS S. F. and HOFMANN A. F. (1971) Colonic secretion of water and electrolytes induced by bile acids: perfusion studies in man. *J. Clin. Invest.* **50**, 1569–1577.

MIETTINEN T. A. (1971) The role of bile salts in diarrhoea of patients with ulcerative colitis. *Gut* **12**, 633–635.

NIELSEN J. R. (1964) The development of cholelithiasis following vagotomy. *Am. J. Digest. Dis.* **9**, 506–508.

POLEY J. R., HOFMANN A. F. and AMMON H. V. (1972) quoted by HOFMAN A. F. (1972) Bile acid malabsorption caused by ileal resection. *Arch. Intern. Med.* **130**, 597–605.

REYNOLDS R. M. (1962) cited by GRIFFITH C. A. (1962) Selective gastric vagotomy. *West J. Surg.* **70**, 175–180.

ROW G. G. (1967) Control of tenesmus and diarrhoea by cholestyramine administration. *Gastroenterology* **53**, 1006.

RUDICK J. and HUTCHINSON J. S. F. (1964) Effect of vagal nerve section on the biliary system. *Lancet* **1**, 579–581.

SABUROV G. E. (1961) The effect of vagotomy on the bile secretion function of the liver. *Sechenov Physiol. J. USSR* **47**, 685–692.

SJOVALL J. (1959) On the concentration of bile acids in human intestine during absorption. *Acta Physiol. Scand.* **46**, 339–345.

SMITH D. C., MACKAY C. and MCALLISTER R. A. (1973) The effect of vagotomy and drainage on the composition of bile. *Scott. Med. J.* **18**, 65–66.

SOBOTKA H. H. (1937) *Physiological Chemistry of Bile.* London, Baillière, Tindall & Cox.

STANLEY M. M. and NEMCHAUSKY B. (1967) Fecal C^{14} bile acid excretion in normal subjects and patients with steroid wasting syndromes secondary to ileal dysfunction. *J. Lab. Clin. Med.* **70**, 627–639.

VAN DEEST B. W., FORDTRAN J. S., MORAWSKI S. G., WILSON J. D. (1968) Bile salt and micellar fat concentration in proximal small bowel contents of ileectomy patients. *J. Clin. Invest.* **47**, 1314–1324.

Br. J. Surg. Vol. 62 (1975) 313–316

Possible parathyroid origin of gastrin in a patient with multiple endocrine adenopathy type I

J. CASSAR, J. M. POLAK AND W. M. COOKE*

SUMMARY

After removal of two large pancreatic insulinomas, although the presenting spontaneous hypoglycaemia was eliminated, severe and persisting haematemesis and melaena supervened with a rise in serum gastrin. The patient had multiple endocrine adenopathy (pituitary, parathyroids and islet cells), but no evidence of a pancreatic gastrin-producing tumour. After emergency gastric operation for the bleeding, the serum gastrin remained high until the hypercalcaemia and hyperparathyroidism had been corrected by subtotal parathyroidectomy. Immunofluorescence studies showed gastrin in the parathyroid tissue.

MULTIPLE endocrine adenopathy type I is characterized by tumours or hyperplasia of the parathyroids, pancreatic islets, pituitary, adrenal cortices and the thyroid gland (Ballard et al., 1964; Steiner et al., 1968). A patient with some unusual features and the results of special investigations are reported.

Case report

A 52-year-old Indonesian head teacher was admitted to Hammersmith Hospital in May 1973. She had noted enlargement of the feet since 1942. In 1963 she had become confused before breakfast and had had blackouts, preceded by cold sweats, when meals were delayed, and consequently had given up her job. She had been referred to a psychiatrist and found to be hypoglycaemic and acromegalic in 1965.

In 1967, in Paris, she had had cobalt radiation (3000 rad) to the pituitary gland. Frequent sweet drinks and injections of glucagon had also been advised because of continuing hypoglycaemic attacks. In February 1973, when diazoxide 150–200 mg per day had been started, she had had no further blackouts and her fasting blood glucose, which before treatment had been in the 30–35 mg/100 ml range, had risen to 112–120 mg/100 ml. One of her brothers and one of her sons had had renal calculi and another of her brothers may have had renal colic. Two of her children and one of her sisters were investigated at Hammersmith, and in each the fasting blood sugar, tolbutamide test, serum calcium and phosphate and skull X-rays were normal.

On admission the patient was obviously acromegalic, but further examination was unremarkable.

A tolbutamide test (*Fig.* 1) was started with the patient hypoglycaemic† (fasting) but symptomless, and was stopped after 60 minutes because she became drowsy. The serum insulin assays during both the tolbutamide test and an oral glucose test (*Figs.* 1, 2) showed fasting hyperinsulinaemia and grossly exaggerated serum insulin responses. The basal serum growth hormone level was high (68 μu./ml), and during the glucose tolerance test there was a paradoxical rise (*Fig.* 2). A ballooned sella was noted on X-ray of the skull. A pancreatic arteriogram (*Fig.* 3) showed a large vascular mass in the tail of the pancreas and another probable lesion in the body. Barium meal examination and liver scan were normal. At this time her serum calcium ranged between 11·8 and 12·5 mg/100 ml and the serum phosphate between 3·9 and 4·0 mg/100 ml. The serum alkaline phosphatase was 97–115 u./l. Plasma parathormone levels were 740, 790 and 990 pg/ml (normal <730 pg/ml). Plasma calcitonin was normal (<100 pg/ml). Gastric secretion was normal: basal acid output 2·1 mEq/h (normal < 5 mEq/h), peak acid output after pentagastrin 18·3 mEq/h (normal<30 mEq/h) and fasting plasma gastrin 200 pg/ml (normal<100 pg/ml). Thyroid-stimulating hormone response to thyroid-releasing hormone was normal and so were her luteinizing hormone and follicle-stimulating hormone responses to luteinizing-releasing hormone. Serum thyroxine was 90 ng/ml (normal 55–115 ng/ml). The plasma cortisol increased to 40 μg/100 ml in response to hypoglycaemia.

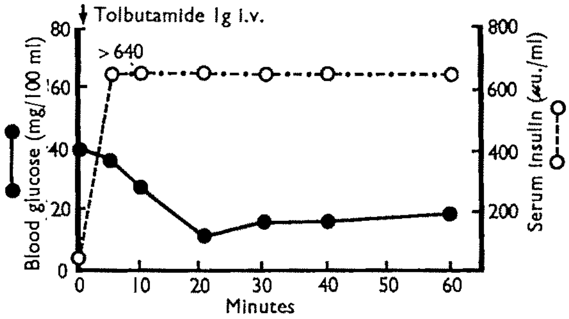


Fig. 1. Preoperative tolbutamide test.

At operation on 31 May 1973 (Professor R. B. Welbourn) a tumour approximately 10 cm in diameter was found in the tail of the pancreas and one about 3 cm in diameter in the body. The body and tail of the pancreas and the spleen were resected. One week after operation the fasting blood glucose was 155 mg/100 ml. Shortly after her discharge from hospital she was readmitted as an emergency with epigastric pain, haematemesis and melaena. She was shocked and her haemoglobin was 8·4 g/100 ml. Barium meal examination showed no ulceration and gastroduodenoscopy revealed no cause for the bleeding. The melaena continued and on 16 June a large bleeding ulcer in the first part of the duodenum was underrun and a truncal vagotomy and pyloroplasty carried out (Professor R. B. Welbourn). She was admitted yet again on 11 July with epigastric pain and melaena, when her haemoglobin was 6·4 g/100 ml. Endoscopy showed blood clot adherent to the posterior wall of the duodenum but no active bleeding. However, massive melaena continued and an antrectomy, with a Polya anastomosis, was done on 12 July (Professor R. B. Welbourn). Thereafter she had only minor epigastric discomfort and no further bleeding. The levels of gastric acid secretion and plasma gastrin are shown in *Table I*.

An air encephalogram on 26 September showed extension of the subarachnoid space into the pituitary fossa, implying some necrosis of her pituitary tumour, as suggested by a fall in the growth hormone level (7·9 μu./ml on 10 September). She was therefore treated with external radiotherapy (4000 rad) over 4 weeks, starting on 7 October. At the beginning of

---

*Departments of Medicine, Histochemistry and Surgery, Hammersmith Hospital and Royal Postgraduate Medical School, London.

† Blood glucose was measured by a Technicon Auto-Analyser 1 using ferricyanide reduction based on the method of Hoffman (1937).

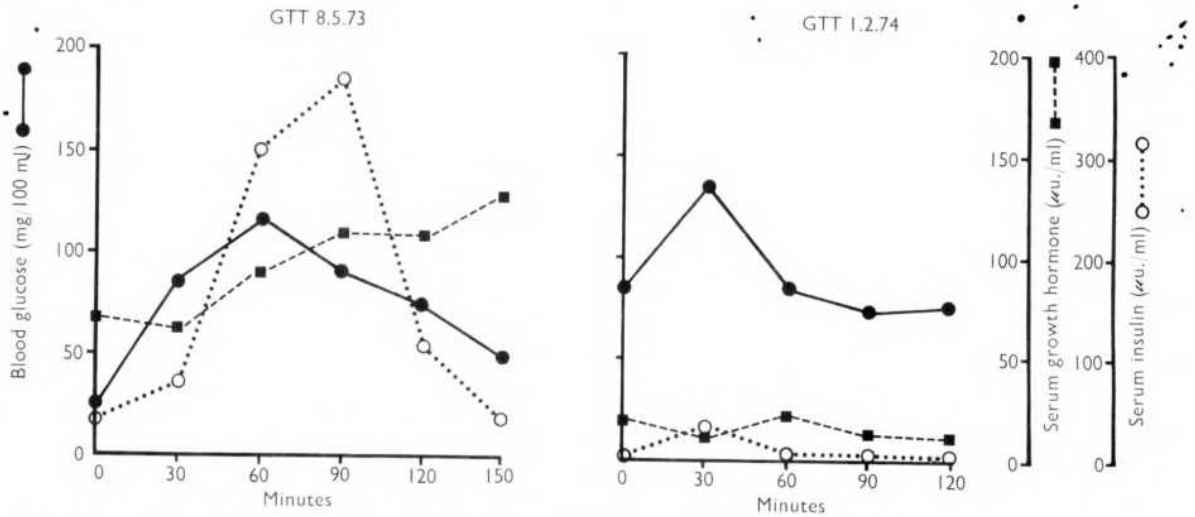


Fig. 2. Glucose tolerance tests with serum insulin and growth hormone assays before and after treatment.

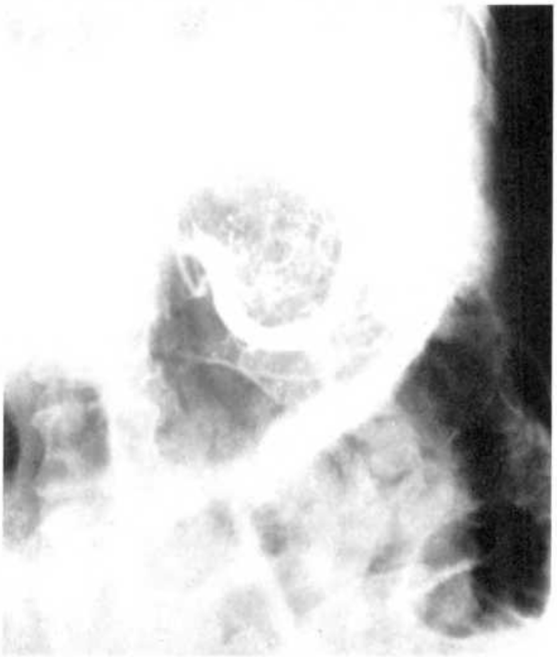


Fig. 3. Splenic arteriogram showing the abnormal blood vessels (surrounded by the splenic artery) of the insulinoma.

November she was still hypercalcaemic (12·1 and 12·4 mg/100 ml) and the urinary calcium excretion was 0·35 and 0·19 g in 24 hours.

She was thought to have hyperparathyroidism, and exploration of her neck on 18 December (Mr Selwyn Taylor) showed four enlarged parathyroid glands. The left upper and right lower glands were removed totally, and four-fifths of the other two were removed also. Recovery was uneventful and she had no further epigastric pain or discomfort. Two weeks post-operatively her serum calcium was 8·8 mg/100 ml.

On 1 February 1974 a glucose tolerance test (*Fig.* 2) showed normal glucose values, a normal serum insulin response and moderately raised serum growth hormone levels, although now reduced to about one-sixth of the pretreatment level of growth hormone. The patient was also symptom-free and she returned to her home country.

Table 1: GASTRIC SECRETION STUDIES AND SERUM GASTRIN LEVELS

Date	Surgery	BAO (mEq/h)	PAO_{PG} (mEq/h)	Fasting gastrin (pg/ml)
22.5.73		2·1	18·3	200
31.5.73	Distal pancreatectomy			
11.6.73	Truncal vagotomy + pyloroplasty			
4.7.73		11·6	20·6	
12.7.73	Antrectomy			
31.7.73		3·1	11·3	538
		Insulin negative		
2.10.73				237
7.10.73	Radiotherapy to pituitary gland			
21.11.73				160
18.12.73	Parathyroidectomy			
31.12.73				41
29.1.74		Nil	6·2	
		Insulin negative		

BAO, Basal acid output. PAO_{PG}, Peak acid output in response to pentagastrin.

Biopsies were processed for histological, cytochemical and immunohistochemical studies and for electron microscopy, as described previously (Pearse and Polak, 1974; Pearse et al., 1974). Both pancreatic tumours had the typical characteristics of an endocrine tumour with polygonal and round cells forming masses or glandular structures separated by bands of connective tissue and amyloid deposits. Histological methods for staining endocrine secretory granules (lead haemotoxylin, masked metachromasia, argyrophilia) were all positive. Ultrastructural studies revealed numerous electron-dense round secretory granules which were not identifiable as cell granules. Immunohistochemical studies were done with antisera against the following polypeptides: gastrin, glucagon, insulin, C peptide, secretin, calcitonin, growth hormone, adrenocorticotrophic hormone, GIP, VIP and motilin. Both tumours were reactive only to an antiserum against insulin, and the amyloid was reactive to an antiserum against porcine C peptide. The islet cells of the normal pancreas showed intense positive fluorescence for both insulin and C peptide, but weak reactivity for glucagon and no reactivity for gastrin.

The resected portions of the parathyroid glands weighed 1·24 g. There was diffuse hyperplasia affecting both chief and oxyphil cells. The latter were identified by the presence of numerous mitochondria (mitochondrion-rich cells) and contained electron-dense polymorphic secretory granules predominantly localized towards the vascular poles of the cells. Antiserum against human parathyroid hormone showed reactive chief cells scattered throughout all the glands and concentrated mainly around blood vessels. Most of the oxyphil cells were stained positively with an antiserum against human gastrin I.

The number and distribution of gastrin-producing (G) cells in the antrum were normal. G cells and other endocrine polypeptide cells were also present in biopsies of the duodenal and jejunal mucosa.

Discussion

Duodenal ulceration is common in multiple endocrine adenopathy type I even in the absence of a gastrinoma (Ballard et al., 1964). A barium meal examination before the first operation showed no duodenal ulceration, and it is a matter for speculation why haematemesis and melaena occurred soon after the distal pancreatectomy. Although the preoperative gastrin level was raised, the value after pancreatectomy, vagotomy and antrectomy was even higher. This is contrary to the usual fall after resection of the gastric antrum (Stadil, 1974). Thereafter the gastrin level fell steadily but returned to normal only after parathyroidectomy.

The source and cause of the marked hypergastrinaemia remain puzzling. Acute insulin-induced hypoglycaemia is a powerful stimulant of gastric acid secretion and gastrin release. Hypoglycaemic attacks produced by the insulinoma are unlikely to have caused the initial high gastrin value which was greater than that produced by the intravenous administration of insulin (Korman et al., 1971). Long standing chronic hyperinsulinaemia may well be very different. Under certain conditions insulin may inhibit gastric secretion (Spencer, 1973), and the coexistence of a duodenal ulcer and an islet cell tumour producing hypoglycaemia is rather unusual (Janowitz and Crohn, 1951). However, Ward and Welbourn (1961) showed that gastric secretion in a patient with an insulinoma was responsive to spontaneous hypoglycaemia.

Gastric acid secretion may be stimulated by the intravenous infusion of calcium, and recently Reeder et al. (1970) have increased plasma gastrin in this way in patients without the Zollinger–Ellison syndrome. Hypercalcaemia may have been responsible for the hypergastrinaemia in our patient, but if so the fall after antrectomy and prior to the parathyroidectomy is puzzling. An association between peptic ulceration, increased basal acid output and hyperparathyroidism with a return to normal basal secretion after parathyroidectomy has frequently been noted (Ward et al., 1964; Barreras and Donaldson, 1967; McGuigan et al., 1974). Dent et al. (1972) found elevated gastrin values in 8 out of 18 patients with hyperparathyroidism, with return to normal after surgery. Polak et al. (1971) have shown hyperplasia of the antral G cells in patients with primary hyperparathyroidism, but there was no such hyperplasia in our patient. The final normal gastric secretion test suggested that the parathyroidectomy had reduced gastric acid secretion, although part of this decrease may have been due to other factors including the reduction of the growth hormone level. There is evidence in man that gastric secretion is increased in acromegaly (Hall, 1971) and decreased in hypopituitarism (Smith et al., 1961) and after hypophysectomy (Dotevall and Westling, 1963). Growth hormone has been shown to increase gastric secretion to normal after hypophysectomy in rats (Kyle and Welbourn, 1956).

The finding of gastrin-like immunofluorescence in the oxyphil cells of the parathyroid is extremely interesting and suggests that these cells were the source of gastrin (Stremple and Watson, 1974). In the absence of direct measurements in the blood vessels supplying the parathyroid glands it is not possible to exclude absorption by the cells from the high level of circulating gastrin.

A gastrinoma could be another cause of the hypergastrinaemia, but despite a careful search there was no evidence of increased G cells in the antrum or duodenum or of a residual islet cell pancreatic tumour (although this cannot be excluded), and the plasma gastrin level eventually fell to normal. In spite of the increased serum gastrin, the preoperative gastric acid values were within normal limits. It is difficult to explain the rise in the basal acid output and the absence of a fall in the peak acid output after the pancreatectomy, truncal vagotomy and pyloroplasty. We failed to demonstrate hormones other than insulin, which may have had an inhibitory effect on gastric acid secretion, in immunocytochemical studies of the tumour.

The insulinoma showed characteristics typical of an apudoma (Pearse and Welbourn, 1973). The tumour reacted less strongly to an antiserum against insulin than is usual for insulinomas, but this fact and the presence of secretory granules uncharacteristic of beta cells have been well documented (Creutzfeldt et al., 1973). Amyloid is found in many endocrine polypeptide tumours and there is evidence that this apudamyloid is different from that found in secondary amyloidosis (Pearse et al., 1972).

Some acromegalics develop pituitary apoplexy spontaneously and an air encephalogram may show a partly empty sella and lowered growth hormone level, as in the present case. The air encephalogram after her operation showed extension of the subarachnoid space into the pituitary fossa with an empty sella. This is, of course, a sella partly empty because the tumour has shrunk, rather than a true empty sella syndrome (Neelon et al., 1973). Similar infarcts may well be precipitated by a series of shock states from gastric bleeds such as our patient suffered. Our patient early after her radiotherapy was still mildly acromegalic clinically and by serum growth hormone levels, but longer follow-up may well show considerable further late improvement (Gordon and Roth, 1973).

Acknowledgements

We wish to thank Professor Russell Fraser, Professor R. B. Welbourn and Mr Selwyn Taylor for encouraging us to publish details of their patient and for their helpful criticism of this report. We are grateful to Professor R. E. Steiner for the arteriogram, Professor

A. G. E. Pearse in whose laboratory the histochemical studies were made, Dr S. R. Bloom for the assays of gastrin, Professor W. Creutzfeldt for the donation of the antiserum to porcine C peptide and Miss S. Nichols for secretarial assistance.

References

BALLARD H. S., FRAME B. and HARTSOCK R. J. (1964) Familial multiple endocrine adenoma–peptic ulcer complex. *Medicine* **43**, 481–516.

BARRERAS R. F. and DONALDSON R. M. (1967) Role of calcium and gastric hypersecretion, parathyroid adenoma and peptic ulcer. *New Engl. J. Med.* **276**, 1122–1124.

CREUTZFELDT W., ARNOLD R., CREUTZFELDT U., DEUTICKE H., FRERICHS H. and TRACK N. S. (1973) Biochemical and morphological investigations of 30 human insulinomas. *Diabetologia* **9**, 217–321.

DENT R. I., JAMES J. H., WANG C., DEFTOS L. J., TALMAO R. and FISCHER J. E. (1972) *Ann. Surg.* **176**, 360–369.

DOTEVALL G. and WESTLING H. (1963) Gastric acid secretion before and after hypophysectomy in man. *Acta Med. Scand.* **174**, 777–780.

GORDON P. and ROTH J. (1973) The treatment of acromegaly by conventional pituitary irradiation. In: KOHLER P. O. and ROSS G. T. (ed.) *Diagnosis and Treatment of Pituitary Tumours.* Excerpta Medica, Amsterdam, p. 230.

HALL W. H. (1971) The parietal cell mass: growth hormone relationship in man. *Am. J. Dig. Dis.* **16**, 139–143.

HOFFMAN W. S. (1937) A rapid photoelectric method for the determination of glucose in blood and urine. *J. Biol. Chem.* **120**, 51–55.

JANOWITZ A. D. and CROHN B. B. (1951) Hyperinsulinism and duodenal ulcer. *Gastroenterology* **17**, 578–580.

KORMAN M. G., SOVENY C. and HANSKY J. (1971) Radioimmunoassay of gastrin. The response of serum gastrin to insulin hypoglycaemia. *Scand. J. Gastroenterol.* **6**, 71–75.

KYLE J. and WELBOURN R. B. (1956) The influence of the adenohypophysis and the adrenal cortex on gastric secretion in the rat. *Br. J. Surg.* **44**, 241–247.

MCGUIGAN J. E., COLWELL J. A. and FRANKLIN J. (1974) Effect of parathyroidectomy on hypercalcaemic hypersecretory peptic ulcer disease. *Gastroenterology* **66**, 269–272.

NEELON F. A., GOREE J. A. and LEBOVITZ H. E. (1973) The primary empty sella: clinical and radiographic characteristics and endocrine function. *Medicine* **52**, 73–92.

PEARSE A. G. E., EWEN S. W. B. and POLAK J. M. (1972) The genesis of apudamyloid in endocrine polypeptide tumours: histochemical distinction from immunoamyloid. *Virchows Arch.* (*Zellpathol.*) **10**, 93–107.

PEARSE A. G. E. and POLAK J. M. (1974) Endocrine tumours of neural crest origin: neurolophomas, apudomas and the APUD concept. *Med. Biol.* **52**, 3–18.

PEARSE A. G. E., POLAK, J. M. and HEATH C. M. (1974) Polypeptide hormone production by "carcinoid" apudomas and their relevant cytochemistry. *Virchows Arch.* (*Zellpathol.*) **16**, 95–109.

PEARSE A. G. E. and WELBOURN R. B. (1973) The apudomas. *Br. J. Hosp. Med.* **10**, 617–624.

POLAK J. M., BUSSOLATI G. and PEARSE A. G. E. (1971) Cytochemical, immunofluorescence and ultrastructural investigations of the antral G cells in hyperparathyroidism. *Virchows Arch.* (*Zellpathol.*) **9**, 187–197.

REEDER D. D., JACKSON B. M., BAN J., CLENDINNEN B. G., DAVIDSON W. D. and THOMPSON J. C. (1970) Influence of hypercalcaemia on gastric secretion and serum gastrin concentrations in man. *Ann. Surg.* **172**, 540–546.

SMITH A. W. M., DELAMORE I. W. and WILLIAMS A. W. (1961) Gastric acid secretion and mucosal appearances in Addison's disease and hypopituitarism. *Gut* **2**, 163–167.

SPENCER J. (1973) Inhibition of gastric secretion by insulin. *Scand. J. Gastroenterol.* **8** (*Suppl.* 21).

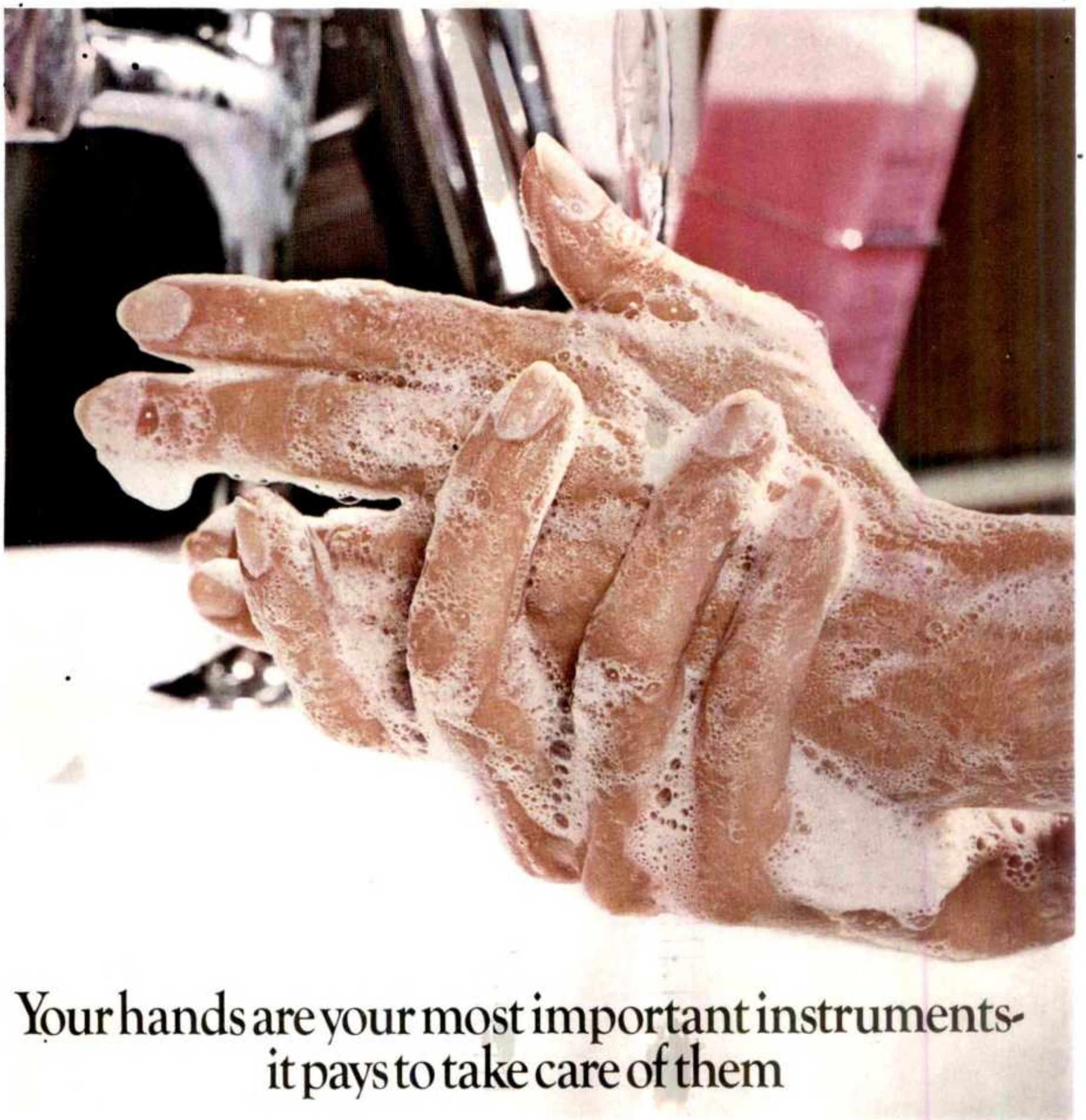
STADIL F. (1974) Gastrin and insulin hypoglycaemia. *Scand. J. Gastroenterol.* **9** (*Suppl.* 23).

STEINER A. L., GOODMAN A. D. and POWERS S. R. (1968) Study of a kindred with phaeochromocytoma, medullary thyroid carcinoma, hyperparathyroidism and Cushing's disease. Multiple endocrine neoplasia, Type II. *Medicine* **47**, 371–409.

STREMPLE J. F. and WATSON G. C. (1974) Serum calcium, serum gastrin, and gastric acid secretion before and after parathyroidectomy for hyperparathyroidism. *Surgery* **75**, 841–852.

WARD J. T., ADESOLA A. O. and WELBOURN R. B. (1964) The parathyroids, calcium and gastric secretion in man and the dog. *Gut* **5**, 173–183.

WARD J. T. and WELBOURN R. B. (1961) Gastric secretion in organic hyperinsulinism. *Lancet* **2**, 986–987.



Your hands are your most important instruments-
it pays to take care of them

The obvious fact that a urgeon's hands are of prime mportance to his work was orne in mind when 'Hibiscrub' vas formulated. 'Hibiscrub' is lesigned to keep hands healthy, ven after repeated use.

However, the prime mportance of a handwash is effectiveness: rapid prolonged bactericidal action against skin bacteria is assured by the presence of the well-proven antiseptic 'Hibitane'.

"These studies have shown that a 4% chlorhexidine detergent solution ['Hibiscrub'] is a potentially outstanding addition to the small list of detergent-disinfectant preparations for the hands of surgeons and nurses, with a greater immediate effect than that obtained with the hexachlorophane or even the iodophor preparations."
British Medical Journal, (1973), 1, 510.

hibiscrub

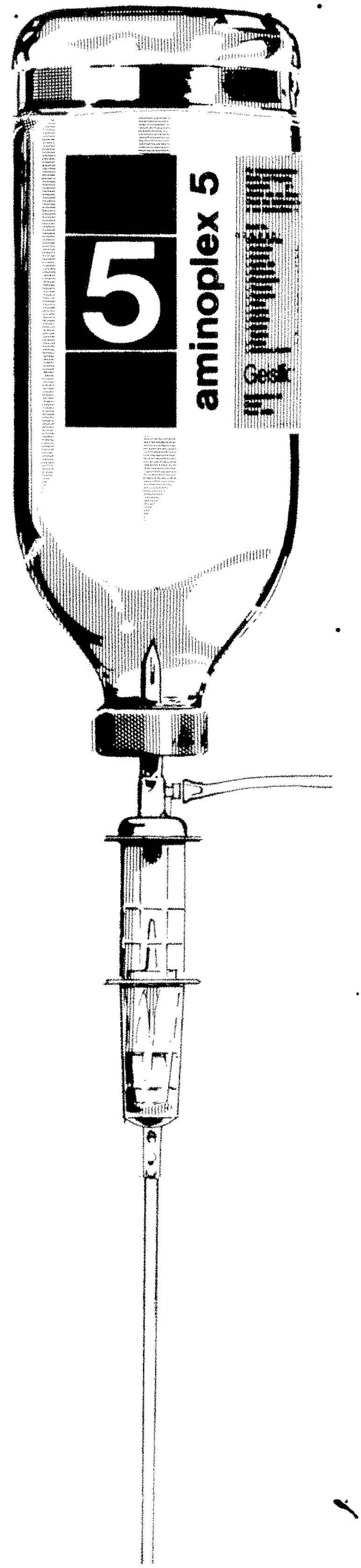
RAPID BACTERICIDAL SKIN CLEANSER

Contains 'Hibitane' Chlorhexidine Gluconate 4% w/v.

ICI Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

'Hibitane' and 'Hibiscrub' are trade marks.

PH828



The single solution
for parenteral nutrition

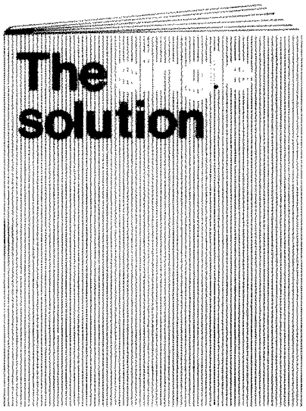
Aminoplex 5

1 litre three times per day
provides 15g. of utilisable
nitrogen and 3000K calories;
the nutrient content being
derived from synthetic
L-Form amino acids,
sorbitol and alcohol.

Geistlich
Chester

In co-operation with Salvia-Werk
G.m.b.H., Homburg/Saar, W.Germany.

Medical literature
available from:
Geistlich Sons Ltd.,
Newton Bank,
Long Lane,
Chester CH2 3QZ.
Telephone
Chester 47534-7



Br. J. Surg. Vol. 62 (1975) 317–319

The cholecystokinin test: an assessment

D. R. K. REID, I. M. ROGERS AND J. F. CALDER*

SUMMARY

A cholecystokinin (CCK) test was performed on 13 female patients who were thought to be having attacks of gallbladder pain and in whom at least one cholecystogram had been normal. In 10 of these patients the CCK test was performed during the course of a repeat cholecystogram in order to assess the effect of CCK on gallbladder contraction.

There was no constant relationship between a positive test and gallbladder contraction as measured radiographically.

Cholecystectomy was undertaken in 9 patients and of these, 4 had been CCK positive, 4 had been CCK negative and 1 had reacted equivocally. None of the CCK positive patients had stones at operation, whereas 2 of the CCK negative patients had one or two small stones. In this small series cholecystectomy relieved both the CCK negative and CCK positive patients of pain with equal frequency.

It is concluded that a negative CCK test by no means excludes the presence of symptomatic gallstones in patients with X-ray negative gallbladder pain.

PREVIOUS reports have shown that severe and recurrent gallbladder pain may be experienced when the cholecystogram is perfectly normal (Cozzolino et al., 1967; Valberg et al., 1971; Reid and Rogers, 1975). It is, however, not uncommon to find that the clinician will absolve the gallbladder as the source of the pain when the cholecystogram is normal and will undertake investigations designed to reveal pathology in other organs. Clearly a test which would confirm or refute clinical suspicion of X-ray negative gallbladder pain would be of considerable value.

Such a test was introduced in 1963 by Cozzolino et al. and is called the cholecystokinin (CCK) test. The test is stated to be positive when a typical attack of gallbladder pain occurs within 10 minutes of the intravenous injection of 1·5 Ivy units/kg of CCK. The value of this test has been assessed by several authors (Nathan et al., 1969; Valberg et al., 1971) and there is general agreement that in patients considered to have X-ray negative gallbladder pain a positive test will usually mean that cholecystectomy will relieve the attacks of pain whatever the operative or histological findings. However, there is no such agreement about the significance of a negative CCK test, although Nathan et al. (1969) made the unsubstantiated claim that about 40 per cent of patients with proved biliary disease are negative reactors. No positive CCK tests have been documented among patients used as normal controls (Cozzolino et al., 1963; Valberg et al., 1971).

The present small prospective analysis was designed to investigate further the significance of the CCK test in patients thought to have X-ray negative gallbladder pain.

Materials and methods

Thirteen female patients between the ages of 19 and 60 years who were thought to be having attacks of gallbladder pain despite a normal cholecystogram were studied. The duration of symptoms ranged from 8 months to 10 years.

Each patient had a CCK provocation test, and in 10 cases this was carried out during the course of an oral cholecystogram so that the effect on gallbladder contraction could be observed. In every case at least one normal routine oral cholecystogram had been obtained before the test was contemplated. The technique of the test was as follows.

The patients were told that they would be having another cholecystogram and that an injection would be administered to them during the X-rays. It was not suggested that the injection might provoke pain. Prone, prone-oblique and erect films were taken 14 hours after the ingestion of 6 tablets of iopanoic acid (Telepaque). Cholecystokinin/pancreozymin (Boots) was injected over a period of 1 minute and further prone or prone-oblique films were taken at 2, 4, 6, 8 and 20 minutes after the start of the injection. The injection of 1·5 Ivy units/kg of CCK was made into the tubing of an intravenous saline infusion set up behind the patient so that she was not made aware of the moment of injection, and the test was considered positive when typical pain was experienced within 10 minutes of the injection.

The decision about cholecystectomy was made on clinical grounds without reference to the result of the test although this information was not specifically withheld from the surgeon.

Results

Surgery was thought to be clinically indicated in 9 cases and cholecystectomy was carried out. There were 4 CCK positive and 4 CCK negative patients in this group and 1 patient had displayed an equivocal reaction (*Table I*).

CCK positive patients

It can be seen by reference to *Table I* that only one of the positive reactors was not relieved of her attacks of pain by cholecystectomy. It became clear after operation that there was a large functional overlay with this patient (Miss I. R.), but we decided to include her in the series since her initial presentation had appeared convincing. The remaining 3 patients

---

* Royal Infirmary, Glasgow.

Table I: DETAILS OF THE PATIENTS WHO UNDERWENT CHOLECYSTECTOMY

Case	Age	Duration of pain*	CCK test	Cholecystography†	Pathology	Follow-up
Mrs K. D.	28	8 mth; jaundice	+	NAD × 2	Mild chronic cholecystitis	Pain-free; 9 mth
Miss M. M.‡	54	3 yr; jaundice	+	NAD × 2	Normal	Pain-free; 12 mth
Mrs N. G.	60	1 yr	+	NAD	Normal	Pain-free; 18 mth
Miss I. R.	49	10 yr	+	? Septum in gallbladder	Loculated gallbladder	Continuing pain; 9 mth
Mrs S. H.	23	10 mth; jaundice	±	NAD × 2	Mild chronic cholecystitis, a few cholesterol stones	Pain-free; 7 mth
Miss A. L.	26	3 yr	−	NAD × 2	Loculated gallbladder	Pain-free; 12 mth
Mrs G. G.	46	5 yr	−	NAD × 2	One cholesterol stone	Continuing pain; 4 mth
Mrs M. C.	49	1 yr; jaundice	−	NAD × 2	Mild chronic cholecystitis, 2 cholesterol stones	Pain-free; 12 mth
Mrs M. C.	36	11 mth	−	NAD	Chronic cholecystitis	Pain-free; 12 mth

* In 4 cases jaundice or dark urine and pale stools had occurred during one of the attacks of pain.
† The number of cholecystograms indicated includes the cholecystogram associated with the CCK test.
‡ Appendicectomy was performed during cholecystectomy.

Table II: DETAILS OF THE PATIENTS WHO DID NOT UNDERGO CHOLECYSTECTOMY

Case	Age	Duration of pain	CCK test	Cholecystography	Follow-up*
Miss A. M.	19	2 yr	−	NAD	Continuing pain; 1 yr
Mrs S. C.	37	1 yr	−	NAD	Lost to follow-up
Mrs C. P.	55	10 yr	−	NAD × 2	Pain-free; 4 mth
Mrs J. C.	39	2 yr	−	NAD	Continuing pain; 6 mth
Mrs G. M.	28	2 yr†	+	NAD‡	Continuing pain; 1 yr

* Follow-up was the period of observation after the initial presentation.
† Continuing pain after a previous cholecystectomy.
‡ Intravenous cholangiogram.

experienced immediate and complete freedom from pain after the cholecystectomy. On histological examination 2 of the gallbladders were normal, 1 showed mild chronic cholecystitis and 1 was loculated.

CCK negative patients

Three of the 4 negative reactors were similarly relieved of their pain by cholecystectomy (*Table I*). In one instance (Mrs M. C.) the CCK test was negative on the day before two small cholesterol stones were found within the gallbladder at operation. The patient not relieved of pain by cholecystectomy (Mrs G. G.) had one small cholesterol stone at operation, and it is conceivable that there is a residual small stone in the common bile duct to account for her continuing pain. On histological examination 2 of the gallbladders contained one or two small stones, 1 showed mild chronic cholecystitis and 1 was loculated.

The only patient with an equivocal CCK test had a few small cholesterol stones at operation and has had no postoperative attacks of pain (Mrs S. H.). In all the cases the gross appearance of the gallbladder at operation was normal.

Non-operated patients (*Table II*)

Cholecystectomy was thought not to be indicated in 4 patients because of the mild nature of their symptoms. All of these patients had been negative CCK reactors and had displayed a variable pattern with regard to pain during the period of observation. During the course of investigations a duodenal ulcer was revealed in one patient (Mrs J. C.) and this was treated by total truncal vagotomy and pyloroplasty. The attacks of pain, however, were typical of gallbladder colic and these were continuing when she was reviewed 6 months after the operation.

One patient (Mrs G. M.), who was not included in the series, presented 2 years after cholecystectomy for stones with what appeared to be typical biliary colic. Intravenous cholangiography was normal. The CCK test without X-ray control was positive and she continued to have troublesome colic during 1 year's observation.

Gallbladder contraction

Good gallbladder contraction in response to CCK was observed in only 3 patients (Miss M. M., Mrs C. P. and Miss I. R.). The other patients all showed only slight to moderate contraction. Only one case (Miss M. M.) showed a contraction as good as would be expected after a fatty meal.

Discussion and conclusions

It has already been established that gallstones may be expelled by passage through the biliary tree (Gray, 1974). Indeed, these 'disappearing stones' may account for a clinically significant proportion of patients who present with typical gallbladder colic but have a normal cholecystogram, and the patients in this series without stones at operation may be considered as possible examples (Reid and Rogers, 1975).

The significance of a positive CCK test

If we exclude Miss I. R. on the grounds of functional overlay then all the positive reactors were relieved of their pain by cholecystectomy. When stones are not present at operation we would suggest that the postoperative freedom from pain is because a stone-forming gallbladder has been removed.

The only other positive reactor (Mrs G. M.) had already undergone cholecystectomy and continued to have troublesome colic over 1 year's observation. One possible explanation for her pain would be a residual common duct stone.

There was some correlation between the clinical decision to operate and a positive CCK test in that all the positive reactors with a gallbladder *in situ* were in the operated group.

The significance of a negative CCK test

It is clear from consideration of the operated cases (*Table I*) that a negative CCK test does not absolve the gallbladder as the source of pain. Indeed, the yield of pathological abnormality was greater in the negative cases than that of the positive group and the postoperative freedom from pain was equally convincing.

No correlation could be found between the extent of gallbladder contraction and a positive test. This finding is at variance with that of other authors (Nathan et al., 1969) but is in agreement with the observations of Valberg et al. (1971).

It is concluded that the CCK test without further associated radiology may be a useful ward aid to diagnosis when the cholecystogram is normal. A positive test would tip the balance towards cholecystectomy. No real conclusion can be drawn from the negative test.

Acknowledgements

Two of our cases were under the care of Mr T. Menzies and Mr John Hutchison, Consultant Surgeons at the Royal Infirmary, Glasgow, and we are grateful to them for allowing us to report these cases.

Dr J. Duncan allowed us to use the services of the Radiology Department for the tests.

References

COZZOLINO H. J., GOLDSTEIN F., GREENING R. R. and WIRTS C. W. (1963) The cystic duct syndrome. *JAMA* **185**, 100–104.

GRAY R. (1974) Disappearing gallstones: report of 2 cases. *Br. J. Surg.* **61**, 101–103.

NATHAN M. H., NEWMAN A., MACFARLAND J. and MURRAY D. J. (1969) Cholecystokinin cholecystography. *Radiology* **93**, 1–8.

REID D. R. K. and ROGERS I. M. (1975) The negative cholecystogram in gall-bladder disease. *Br. J. Surg.* **62**. In the press.

VALBERG L. S., JABBARI M., KERR J. W., CURTIS A. C., RAMCHAND S. and PRENTICE R. S. A. (1971) Biliary pain in young women in the absence of gallstones. *Gastroenterology* **60**, 1020–1026.

Br. J. Surg. Vol. 62 (1975) 320–322

Intra-abdominal symptoms arising from spinal osteophytes

S. S. RAWAT, G. K. JAIN AND H. K. D. GUPTA*

SUMMARY

A case of abdominal pain caused by irritation of a segment of jejunum and another due to irritation of the ureter are reported. In both cases the cause of the irritation was established to be osteophytic growth from the 4th lumbar vertebra. After its excision the symptoms disappeared in both cases. To the best of our knowledge, osteophytes have not been reported before to be the cause of intestinal and ureteric pain, and it is therefore urged that in cases of intractable pain these must be considered as a possible cause.

It is generally accepted that spinal osteophytes do not by themselves produce any symptoms. However, they may produce symptoms when they become large enough to irritate the spinal dura mater, giving rise to a constant backache. Also, when an osteophyte enlarges sufficiently to compress a nerve, symptoms are produced. Pain can also result from the pressure of eroded bone on bone, but in these cases the osteophytes are not the cause of the local pain. The lateral bulges of osteophytes do not press on either the dura or the nerve roots and so produce no symptoms except those as a result of direct pressure on the sacrospinalis. It is commonly believed that the anterior growth of osteophytes does not produce symptoms for similar reasons.

The site of the spur, its size, the width of the canal and the amount of pressure determine the severity of the symptoms, while the segment of the cord or the nerve roots affected determine the symptom pattern. Local pain, radicular involvement, sensory changes, depression and absence of ankle and patellar jerks are the most commonly seen consequences. Intermittent claudication made worse by exertion is also seen. Sphincteric disturbances are, however, not common. Pressure on the trachea and oesophagus can produce symptoms, pressure on the vertebral artery may occasion cerebrovascular symptoms and spondylotic changes in the cervicothoracic spine may produce pain which closely simulates angina.

No reports have been found in the literature of cases in which symptoms were produced as a result of pressure of vertebral osteophytes on the ureter or intestine. Two such cases are presented here.

Case reports

Case 1: A 49-year-old Hindu female was admitted to the Dr S. N. Medical College Hospital, Jodhpur, on 12 December 1973 complaining of pain in the abdomen of 1½ years' duration. The pain was para-umbilical and of a dull aching nature. The intensity of the pain was worse after food. Occasionally the pain increased in severity and assumed a colicky character. These attacks were short, lasting an hour or so, and subsided without treatment. On examination there were three scars (result of branding with red hot metal) in the left para-umbilical area. There was deep-seated tenderness 2 cm below the umbilicus on the left side. In the same area a hard immobile mass 2 × 2 cm was palpable in close proximity to the vertebral bodies. No other abnormality was detected. The stools, urine, barium meal examination and fractional test meal were normal. A plain X-ray showed a sharp bony spur projecting from the upper margin of the 4th lumbar vertebra on its left side (*Fig*. 1). An intravenous pyelogram was normal.

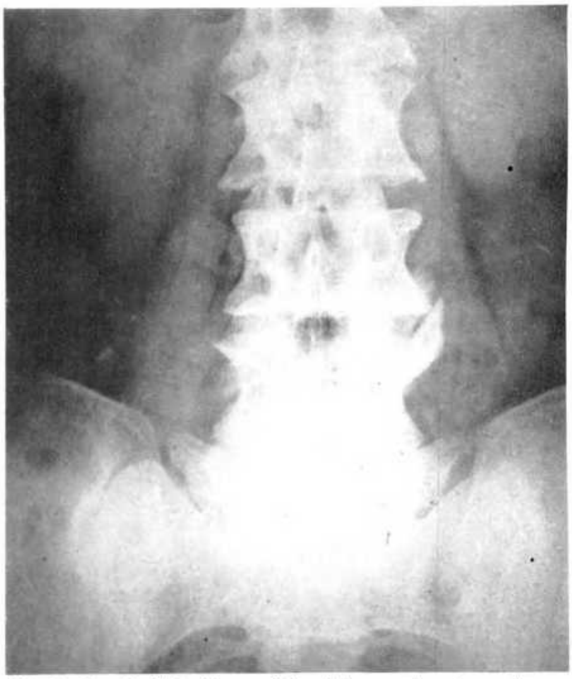


Fig. 1. *Case* 1. Plain X-ray of the abdomen showing a sharp bony spur arising from the upper left margin of the 4th lumbar vertebra. A lateral view was not taken as the condition was not suspected preoperatively to be responsible for the symptoms.

On 20 December the abdomen was explored through a midline incision. The stomach, duodenum, pancreas, gallbladder, colon and appendix were examined and found to be normal. The bony mass on the left side of the 4th lumbar vertebra was found to be projecting sharply anteriorly into the overlying posterior peritoneum. This part of the peritoneum was congested and opaque with scarring. On further examination the posterior aspect of a loop of jejunum 9 cm from the duodenojejunal junction was found to be congested and scarred. This part of the gut lay exactly over the projecting spur. The rest of the small gut was normal. The projecting spur was excised with a rongeur to make it flush with the posterior abdominal wall. The abdomen was closed in layers. The patient was discharged from hospital on 19 January 1974 after

---

* Dr S. N. Medical College, Jodhpur, India.

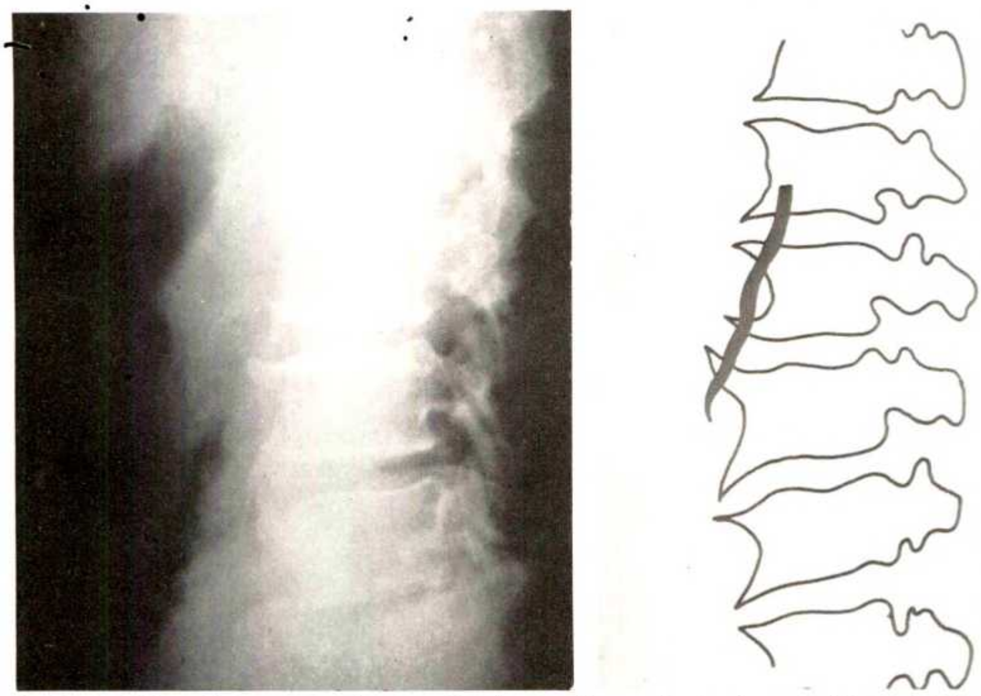


Fig. 2. *Case* 2. Lateral intravenous pyelogram and explanatory diagram showing the ureter lying against the spur.

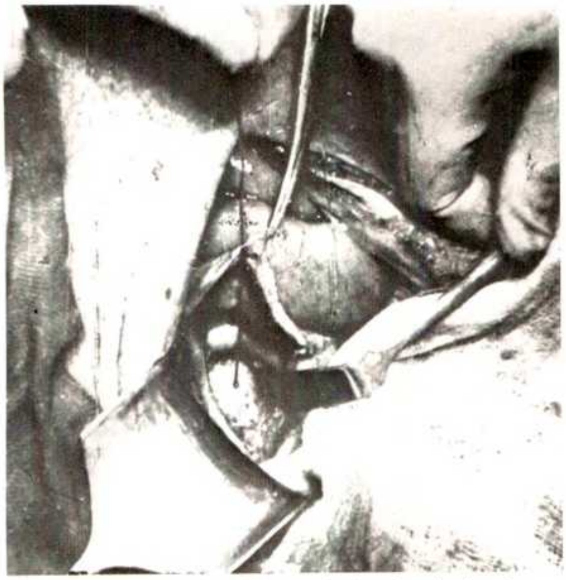


Fig. 3. *Case* 2. Operation photograph showing the tip of a probe touching the projecting spur.

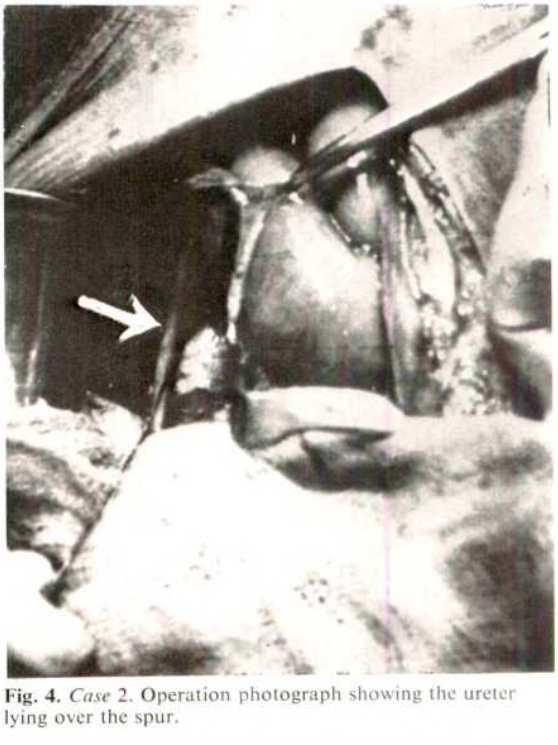


Fig. 4. *Case* 2. Operation photograph showing the ureter lying over the spur.

a 1-month observation period during which she made an uneventful recovery. She has remained symptom-free.

Case 2: A 59-year-old Hindu male was admitted to the Dr S. N. Medical College Hospital on 29 January 1974 complaining of pain in the left hypogastrium radiating to the left scrotum. The pain was constant and dull. Occasionally it became colicky, the colic lasting for about 2 hours in each attack. Physical examination revealed no positive findings. The left para-umbilical region was tender on deep palpation. The urine showed microscopic haematuria. Other laboratory investigations were normal. An anteroposterior X-ray of the abdomen showed osteophytic growth from the 4th lumbar vertebra on its left side. The lateral view showed the spur to be projecting anteriorly. Intravenous pyelography was undertaken to visualize the relationship of the ureter to the osteophyte. The lateral view showed the proximity of the spur to the ureter (*Fig*. 2). The ureter on the left side was lying over the spur; this corresponded with the tender area.

At operation the peritoneum over the spur was found to be scarred and the left ureter was stretched over the spur (*Figs*. 3, 4).

The surface of the ureter for a length of about 2 cm was congested. The anterior projection of the spur was excised with a rongeur. The peritoneum was stitched and the abdomen was closed. Postoperatively the patient was completely relieved of his symptoms and was discharged from hospital after a month's observation, during which he did not experience a recurrence of pain.

Conclusion

We do not suggest that all patients with ill-defined gastro-intestinal or urinary symptoms with spondylosis should be subjected to exploratory laparotomy. This would be a dangerous inference. We would, however, suggest that patients with vague symptoms and anteriorly projecting spurs should be further investigated with the view that such spurs may be the cause of the symptoms in some cases. A palpable spur is highly suggestive.

Br. J. Surg. Vol. 62 (1975) 323–325

Tuberculous peripheral lymphadenitis in the Igbos of Nigeria

WILSON I. B. ONUIGBO*

SUMMARY

Peripheral lymphadenitis is a leading manifestation of tuberculosis. Among the Igbos, who constitute one of the largest ethnic groups in Nigeria, it presents most commonly in the neck, as in other parts of the world. An inguinal presentation, however, is also common. The nodes are often of considerable size. The maximal incidence occurs in the 10–29-year age group, males outnumbering females slightly. It is only in the 40–59-year range that tuberculosis is less common than lymphoma or carcinoma of the peripheral lymph nodes.

Of current concern in England and Wales is the high contribution to tuberculosis notifications from immigrants born in India, Pakistan and the new Commonwealth countries of Africa (Springett, 1972; British Thoracic and Tuberculosis Association, 1973). As reported, the immigrant population dominated in particular the pattern of non-respiratory tuberculosis, especially lymph node tuberculosis. Accordingly, this paper examines the pattern of lymph node tuberculosis from one of the African sources.

The Igbos, who constitute one of the largest ethnic groups in Nigeria (Basden, 1966), are the group studied. Their patterns of peripheral lymph node tuberculosis are compared with those reported recently from England (Hooper, 1972) and India (Krishnaswami et al., 1972).

The present study

One hundred and forty-two surgical specimens showing extrapulmonary tuberculosis were received in formalin at a central laboratory which serves the Igbos who live mainly in the East Central State of Nigeria. They were submitted by 59 doctors working at 5 government, 12 mission and 7 private hospitals during the period February 1970 to June 1974 inclusive.

Histological diagnosis of tuberculosis was based on the finding of typical granulomas with the full picture of caseation, epithelioid cells and Langhans' giant cells.

Analysis revealed 100 individuals with superficial lymph node tuberculosis and 42 with tuberculosis elsewhere (*Table I*).

Age and sex incidence

The age and sex distributions in this series are shown in *Table II*. It is apparent that the maximal incidence occurs in the age group of 10–29 years and that males outnumber females slightly.

Clinical presentation

Thirty-one out of the 100 cases of tuberculous peripheral lymphadenitis presented with a swelling in the neck alone or accompanied by only minor constitutional symptoms (*Tables III, IV*). This was the commonest single finding. It sharply contrasts with the paucity of tuberculosis in the submandibular, submental and tonsillar lymph nodes.

Fifteen cases (*Table III*) showed a particularly acute presentation, i.e. the so-called 'Asian tuberculosis' type. Of these cases, generalized lymph node tuberculosis occurred in 13, hepatomegaly in 7 and ascites in 2 patients.

Table I: SITE OF LESION IN 142 CASES OF EXTRAPULMONARY TUBERCULOSIS

Site of lesion	No. of cases
Superficial lymph node	100
Urogenital tract	17
Peritoneum	12*
Abdominal lymph nodes	8
Skin	5
Bone and joint	2
Soft tissue lesions without underlying bone or joint disease	1
Larynx	1

* Four cases showed peritoneal tuberculosis combined with lesions in the urogenital tract or abdominal lymph nodes.

Table II: AGE AND SEX DISTRIBUTIONS IN 100 CASES OF LYMPH NODE TUBERCULOSIS

Age group	Male	Female	Total
0–9	6	3	9
10–19	12	14	26
20–29	18	14	32
30–39	9	4	13
40–49	4	5	9
50–59	2	2	4
60–69	6	0	6
70+	0	1	1
Total	57	43	100

Inguinal lymph nodes were commonly involved. In addition to the 13 patients with generalized lymph node tuberculosis, 11 manifested the disease in the groin alone, 4 in both the groin and axilla and 3 in the groin and neck together. One case provided a possible clue to the genesis of inguinal lymph node tuberculosis by exhibiting the disease not only in the groin but also in the peritoneum.

Only 4 specimens were so disorganized by abscess formation that they were submitted as necrotic fragments. All 4 were from the neck. The remaining 96 specimens consisted of reasonably well-preserved single or matted nodes which measured from 1 to 7 cm.

---

* General Hospital, Enugu, Nigeria.

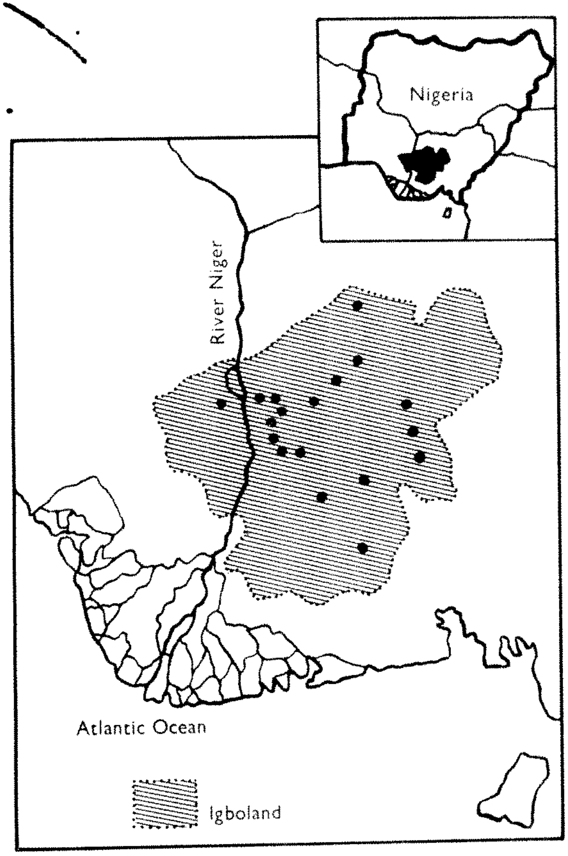


Fig. 1. Map of Igboland showing its relation to the River Niger and (inset) the rest of Nigeria. The relative positions of the hospital towns from which biopsies were sent to the central laboratory are also shown.

Table III: SYMPTOMS AND OTHER FINDINGS

Symptoms and findings	No. of cases
Swelling in neck without other symptoms	25
Swelling in neck with mild general symptoms	6
Swelling in neck accompanied with chest symptoms	14
Swelling in neck with lymph nodes elsewhere affected	21
Acute presentation with high fever, hepatomegaly, etc.	15
Lymph node enlargement with non-lymphoid infection	5

Table IV: SITES OF INVOLVED NODES

Involved site:	No. of cases:
Cervical	56
Axillary	22
Inguinal	18
Submandibular	7
Submental	1
Tonsillar	1
Generalized	13
Unstated	1

Table V: CLINICAL DIAGNOSIS IN 28 CASES NOT DIAGNOSED AS TUBERCULOUS LYMPHADENITIS

Diagnosis:	No. of cases:*
Lymphoma	15
No diagnosis supplied	9
Filariasis	4
Salivary gland tumour	1
Neoplasm	1
Metastasis	1
Hyperplasia	1

* More than one diagnosis was given in some cases.

Of those reaching the considerable size of 3 cm or more, the sites were as follows: neck 15, axilla 10, groin 10 and submandibular region 1. The lateness of the presentation of such cases is well illustrated by the following case history.

Mr O. A., a tailor aged 26 years, first noticed bilateral swellings of the axilla, groin and neck in 1966. The left axillary swelling 'burst' in 1968. By August 1972 the increasing mass and pain in his left groin affected his trade by limiting his use of a pedal sewing machine! When biopsied in October 1972 the specimen consisted of two ovoid enlarged lymph nodes which measured 4·5 and 2·5 cm respectively in their longest axis. On section, the larger node was almost wholly caseous, while the smaller one exhibited scattered caseous foci. Tuberculous granulomas were seen in both nodes microscopically.

Clinical diagnosis

The provisional diagnoses in the 28 cases of this series which were not diagnosed as tuberculosis are listed in *Table V*. A comparison of the cases thought to be due to lymphoma, filariasis or metastasis gives some idea of how doctors rate these conditions among the lumps seen in Igboland.

Diagnostic peripheral lymph node biopsy presents a clear-cut picture of the causes of peripheral swellings in the Igbos (*Table VI*). Tuberculosis is the most common with 100 cases, while lymphoma outnumbers secondary carcinoma by 53 to 24 cases.

Discussion

The traditional therapeutical practices of the Igbos include surgical procedures (Onuigbo, 1955; Basden, 1966). Today, it is not uncommon to see multiple linear scars of lymphadenectomy on the neck, axilla and groin of patients who had consulted the traditional medicine man or 'dibia' at the start of their illness.

In comparison with both the English (Hooper, 1972) and the Indian (Krishnaswami et al., 1972) hospital series, the anatomical distribution in the present series conforms with world-wide patterns in one respect, namely, the predominance of cervical node affliction. It differs pointedly in the relatively high incidence of inguinal node infection. Since account was taken of the possibility of lymphogranuloma venereum, mycosis and other obfuscating diseases, is there a clue to the local prevalence of inguinal tuberculosis? In the present series non-lymphoid extrapulmonary tuberculosis was seen mainly in the peritoneum. It may well

Table VI: AGE DISTRIBUTION OF PATIENTS WITH TUBERCULOSIS, LYMPHOMA OR SECONDARY CARCINOMA IN 177 CASES DIAGNOSED AT PERIPHERAL LYMPH NODE BIOPSY

Age group	Tuberculosis	Lymphoma	Carcinoma
0–9	9	5	0
10–19	26	14	1
20–29	32	4	1
30–39	13	4	3
40–49	9	10	11
50–59	4	9	6
60–69	6	3	0
70 +	1	2	0
Unstated	0	2	2
Total	100	53	24

be, therefore, that the inguinal condition is merely the overt superficial sign of the underlying abdominal disease.

In the English series a node measuring 3 × 2 × 2 cm was cited to illustrate the fact that solid nodes may occasionally attain a considerable size. In the present study, much larger nodes were encountered commonly. They signify that patients present late for treatment and reflect the inadequacy of hospital facilities. *Fig.* 1 shows the distribution of hospital towns from which doctors sent specimens; their sparseness is self-evident.

The age incidence is of interest. In the Igbo series the maximal incidence was in the 10–29-year range, in contrast to the English series (20–39 years) and the Indian series (21–30 years). In other words, younger people are afflicted among the Igbos.

Kilpatrick (1969) pointed out that young people are examined in evaluating the prevalence of tuberculosis in a community and that in one such world-wide study Nigeria ranked sixth out of the 59 countries or areas surveyed. The relative frequency of tuberculous lymphadenitis in young people in the present series is in keeping with this high order of ranking.

The occurrence of tuberculosis in the elderly is also of some importance. In British communities the incidence of peripheral tuberculous lymphadenitis is increasing in the elderly but falling in other age groups (Peel, 1972). The Igbo pattern is probably still stable, for the incidence in the elderly is low.

Table VI shows that it is only in the 40–59-year range that tuberculosis does not outnumber lymphoma or carcinoma. When all age groups are considered the order of incidence in biopsied nodes among the Igbos is: tuberculosis, lymphoma and carcinoma. On the other hand, in the English series carcinoma ranked first and was followed by lymphoma and leukaemia, while tuberculosis came third. Thus, consonant with known epidemiological patterns (MacMahon and Pugh, 1970), the Negro Igbos suffer greatly from infectious diseases, notably tuberculosis.

Since the main theatre of the recent Nigerian civil war (1967–70) was in Igboland, is there any recognizable aftermath in the field of tuberculosis? The author's impression and that of other workers (Pust et al., 1974) is that tuberculosis has increased in the area. Unfortunately, no quantitative answer can be given because all the records which the author collected from 1963 to 1967 were lost during the war.

Acknowledgements

I am grateful to all the doctors who sent me their invaluable specimens and to my technical staff who processed them. I have had helpful discussions with visiting pathologists, especially Dr K. A. Misch and Professors C. V. Harrsion, G. M. Edington, E. O. Odunjo and A. O. Williams. Mazi Kalu Okorie of the East Central State Library Board helped me to locate the map of Igboland which was modified for this paper.

References

BASDEN G. T. (1966) *Niger Igbos.* London, Cass.

BRITISH THORACIC AND TUBERCULOSIS ASSOCIATION (1973) A tuberculosis survey of England and Wales 1971; the influence of immigration and country of birth upon notifications. *Thorax* **54**, 249–260.

HOOPER A. A. (1972) Tuberculous peripheral lymphadenitis. *Br. J. Surg.* **59**, 353–359.

KILPATRICK G. S. (1969) Global tuberculosis. In: HOBSON W. (ed.) *The Theory and Practice of Public Health*, 3rd ed. London, Oxford University Press, pp. 258–259.

KRISHNASWAMI H., KOSHI G., KULKARNI K. G. and JOB C. K. (1972) Tuberculous lymphadenitis in South India—a histopathological and bacteriological study. *Tubercle* **53**, 215–220.

MACMAHON B. and PUGH T. F. (1970) *Epidemiology.* Boston, Little, Brown.

ONUIGBO W. I. B. (1955) Indigenous medical practices of the Ibos of Nigeria. *Glasgow Univ. Med. J.* **21**, 100–110.

PEEL A. L. G. (1972) Peripheral tuberculous lymphadenitis in the elderly. *Br. J. Surg.* **59**, 568–569.

PUST R. E., ONEJEME S. E. and OKAFOR S. N. (1974) Tuberculosis survey in East Central State, Nigeria. *Trop. Geogr. Med.* **26**, 51–57.

SPRINGETT V. H. (1972) Tuberculosis—epidemiology in England and Wales. *Br. Med. J.* **1**, 422–423.

Br. J. Surg. Vol. 62 (1975) 326–329

Gynaecomastia

D. B. HAMER*

SUMMARY

There are two different types of male breast enlargement—gynaecomastia and mammaplasia. A series of 53 consecutive patients with one of these conditions is presented. In the younger age group treatment has usually been conservative, surgery only being advocated when the diagnosis was in doubt or for cosmetic reasons. In the older age group the diagnosis must be confirmed histologically. The incidence of underlying conditions is much higher in this series than in any previously reported.

'GYNAECOMASTIA' is the term commonly used to describe male mammary hypertrophy. Its frequency is increasing because many different drugs are now being shown to be responsible for causing this condition.

There are two clinically separate types which will be referred to as 'true gynaecomastia' and 'mammaplasia'. *Gynaecomastia*: This is characterized by the appearance of well-formed breasts which are similar to those seen in the young adolescent female and are of a similar consistency. Prolonged oestrogen stimulation will produce this appearance (*Fig.* 1).
Mammaplasia: The second type consists of a subareolar plaque of tissue which is much smaller in size and freely mobile, not being attached to the skin or underlying tissues. It is discoid in shape with a regular edge and a rubbery consistency.

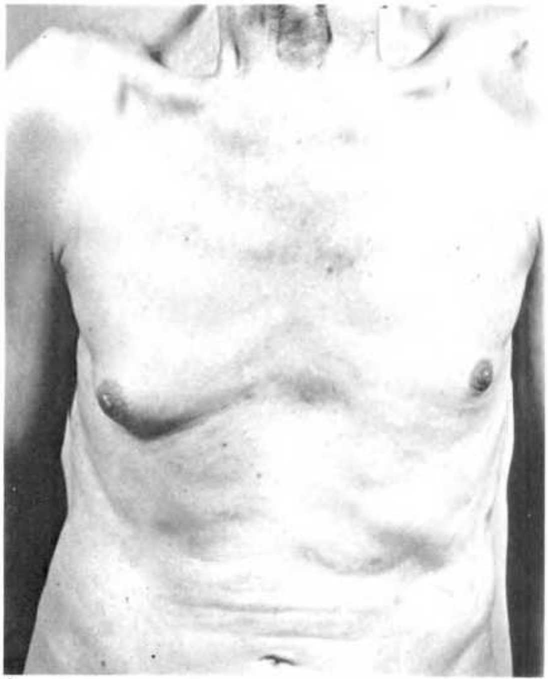


Fig. 1. Patient with oat cell carcinoma of the lung who developed unilateral gynaecomastia.

In mammaplasia or gynaecomastia, regardless of the aetiology, the microscopic findings are similar, with an increase in the ductal and connective tissue elements and no areolar or tubular formation. The pattern is similar to that in the pre-pubertal female breast (Bannayan and Hajdu, 1972).

Investigations

In view of the many underlying conditions a careful and complete examination is essential, with estimations of liver function, urinary oxogenic and ketogenic corticosteroids, biochemical screening, chest X-ray and blood count. The final diagnosis, as always, depends upon histological confirmation. The use of the drill biopsy is a useful adjuvant when, for example, a formal excision is not indicated but a diagnosis is required.

Analysis of the present series

This series consists of 53 patients who presented consecutively to the Breast Clinic at Hammersmith Hospital. There were 22 patients (42 per cent) recognized to be suffering from gynaecomastia while 31 (58 per cent) had mammaplasia. The age distribution was similar in both groups. These figures do not corroborate a previous report which maintained that 90 per cent of patients belong to the group defined as suffering from mammaplasia (Dexter, 1956).

Age distribution

The age at which the lesions developed is shown in *Fig.* 2. There is essentially one peak which lies between the ages of 10 and 30 years and includes the time of puberty. Only one case occurred in a prepubertal boy, thus confirming the rarity of this condition in this age group (August et al., 1972).

Laterality

Twelve patients (23 per cent) presented with bilateral breast enlargement (*Fig.* 2). In 16 (30 per cent) the lesion was on the right side, while in 25 (47 per cent) it occurred on the left.

Histology

The diagnosis was confirmed histologically in 37 cases; 31 by excision and 6 by high speed air drill biopsy under local anaesthesia. In 9 patients the lesion regressed without histological confirmation, 2 patients were considered too ill to undergo any extensive investigations, while the remaining 5 patients failed to reattend the outpatients' clinic after preliminary screening and were lost to follow-up.

---

* Department of Surgery, Hammersmith Hospital and Royal Postgraduate Medical School, London.

Associated conditions

In this series 25 patients (47 per cent) developed a mamary swelling without any obvious associated condition. Investigations in the remaining 28 revealed associations which in some cases were responsible for the condition while in others were probably coincidental.

Tables I and *II* list the patients in whom an associated condition was revealed.

Outcome

a. Conservative: Spontaneous regression took place in 9 patients while 5 declined to reattend, probably because the lesions had dispersed. In only one doubtful case was histological confirmation not possible because the patient was too ill to undergo any diagnostic procedure.

b. Surgery: An operation was indicated when the patient with an embarrassing cosmetic deformity which was not resolving requested excision or when the surgeon feared the possibility of malignancy. *Fig.* 3 indicates the patients requiring operation and the age distribution. Excision was carried out in 31 patients (58 per cent). Of these, 14 were suffering from gynaecomastia and 17 from mammaplasia. In the under 30 age group excision was required in 16 of 28 patients (57 per cent), while in those over 30 years of age 15 (60 per cent) required excision.

In all the cases the operation was performed under a general anaesthetic. Special care was taken to ensure that a complete excision was carried out, since a recurrence has been reported in a remnant of breast tissue (Gooel, 1944). Patients with a well-formed gynaecomastia required a submammary incision, while the smaller plaques seen in mammaplasia could be completely removed via a periareolar incision. The nipple was always preserved.

Discussion

The development of breast tissue depends upon the intricate balance of a number of hormones, the most important being oestrogens, progesterones, growth hormone and prolactin. The excessive production, defective excretion or the introduction of drugs which act directly or indirectly via their metabolites may stimulate breast proliferation and disturb this balance.

The observation that breast enlargement developing in the pubertal age group is associated with developmental changes in the size of the testes, penis and formation of pubic hair (Gangai et al., 1967) lends support to the theory that growth hormone is implicated. Three patients had testicular atrophy which is a well-recognized association (LeWinn, 1941; Treves, 1958).

After the Second World War, soldiers returning from Japanese prisoner of war camps developed gynaecomastia, both during their imprisonment and following release and the reintroduction of a normal diet; here again it is likely that an imbalance of hormones was responsible, and that growth hormone played a significant part (Jacobs, 1948). In this report it was shown that 10 per cent of these patients developed breast swellings and that 15 per cent of these subjects had a previous history of mammary enlargement occurring at puberty. Two patients in the present series gave a history of transient breast enlargement at puberty which subsequently recurred at the ages of 25 and 45 years respectively.

Many disorders have been implicated and, as would be expected, a variety of conditions in which there is hormonal imbalance has been shown to have a definite association. For example, hyperthyroidism and hypothyroidism (Wheeler et al., 1953; Becker et al., 1968; Ashkar et al., 1970; August et al., 1972), pituitary disorders (Treves, 1958), testicular tumours and testicular atrophy (Jacobs, 1948; Treves, 1958) and adrenal tumours and adrenal dysfunction (Nicolis

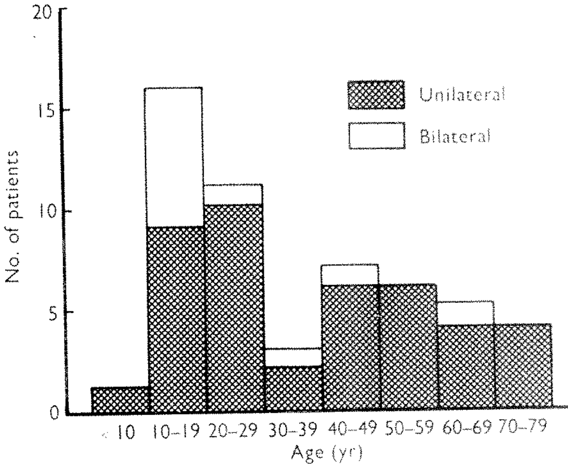


Fig. 2. Incidence of unilateral and bilateral mammary hypertrophy.

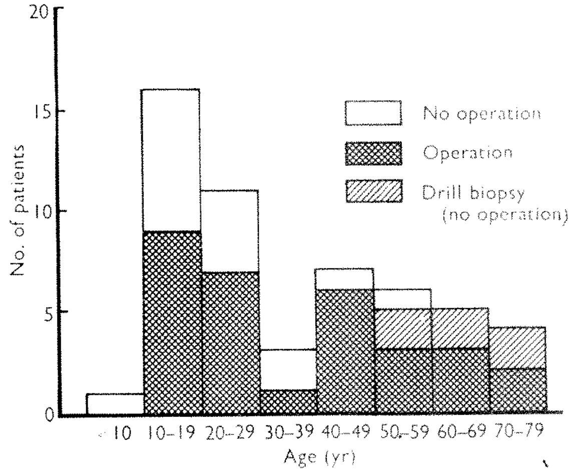


Fig. 3. Incidence of patients requiring operation.

et al., 1971). This problem can also occur in the presence of chromosome abnormality and it is well recognized in Klinefelter's disease (Jacobs, 1948; Wheeler et al., 1953).

Conditions which debilitate the body and upset the normal equilibrium may also cause gynaecomastia or mammaplasia. Disorders of liver function, malnutrition, prolonged immobilization, chronic chest conditions with or without hypertrophic pulmonary osteo-arthropathy, paraplegia, tuberculosis, diabetes mellitus, leprosy, chronic heart disease, hypertension and chronic renal failure are all well-documented causes (Jacobs, 1948; Wheeler, et al., 1953; Keddie and Morris, 1967; Lindsay et al., 1967; Margolis and Gross, 1967; Freeman et al., 1968a, b; Schmitt et al., 1968; Kaminsky, 1969). Male breast enlargement may present not only during the primary disease but also in the recovery period, for example, in malnutrition when refeeding is commenced or in patients with renal insufficiency when dialysis is begun.

In the present series 14 patients (26 per cent) had raised blood urea levels (> 40 mg per cent), pulmonary disease occurred in a further 8 patients and rheumatic heart disease in 3. Diabetes mellitus in patients treated

Table I: ASSOCIATED FACTORS IN PATIENTS WITH TRUE GYNAECOMASTIA

Case no.	Age of onset (yr)	Side	Blood urea nitrogen (mg %)	Associated condition	Associated drugs	Treatment
1	17	R L	—	Sickle cell trait	—	Nil
2	29	L	25	Grand mal	Primidone, acetazolamide, phenytoin, pheneturide	Excision
3	27	L	54	Urea clearance 29 ml/min, creatinine normal, IVP normal	—	Nil
4	37	R L	28	Mitral valve replacement	Spironolactone, frusemide, digoxin, slow K, phenindione	Nil
5	47	L	—	Testicular atrophy, alcoholic, chronic bronchitic	—	Excision
6	52	L	30	Uric acid 10 mg %. Previous two-stage urethroplasty	—	Nil
7	50	R L	44	BSP 13%, enlarged liver, alcoholic	—	Bilateral excision
8	55	R	41	Chronic bronchitic, emphysema, rheumatoid arthritis	Franol, indomethacin, prednisone	Nil
9	62	L	40	Mitral incompetence, coronary thrombosis, ventricular aneurysm previously plicated	Bendrofluazide, digoxin, trinitrin, Warfarin, slow K, chlorpheniramine	Nil
10	61	R L	—	Presented with gynaecomastia, chest X-ray revealed carcinoma of bronchus (oat cell)	Nil	Excision of right side
11	68	R	45	Hypertension, dementia, CVA	Methyldopa, hydrochlorothiazide	Nil
12	76	R	40	Chronic bronchitic	Choledyl, digoxin, frusemide, slow K	Nil

R, Right. L, Left. BSP, Bromsulphthalein. CVA, Cerebrovascular accident.

Table II: ASSOCIATED FACTORS IN PATIENTS WITH MAMMAPLASIA

Case no.	Age of onset (yr)	Side	Blood urea nitrogen (mg %)	Associated condition	Associated drugs	Treatment
1	12	R L	35	Asthma	Promethazine, Intal, oxytetracycline	Nil
2	14	R	—	Petit mal	Acetazolamide, ethosuxamide	Nil
3	18	R L	—	Previously repaired inguinal hernias. Lack of pubic hair, small testes	—	Excision of left side
4	19	L	26	Nephrotic syndrome in remission	—	Nil
5	15	R	45	Undescended left testicle	—	Excision
6	30	R	32	Previous pulmonary tuberculosis	—	Nil
7	41	L	63	Diabetes mellitus treated by diet	—	Excision
8	43	L	38	Diabetes mellitus	Insulin	Excision
9	45	L	25	Testicular atrophy	—	Nil
10	50	L	48	Gastrectomy, vagotomy + Roux-en-Y repair of hiatus hernia	—	Excision
11	52	R	44	Rheumatic heart disease, mitral stenosis, chronic bronchitic	Spironolactone, digoxin, frusemide	Nil
12	55	R	40	Gastrectomy (Polya)	—	Excision
13	64	L	50	Asthma, chronic bronchitic, diabetes mellitus, Paget's disease, nephrosclerosis	Orciprenaline, insulin, chlorpromazine, prednisone	Excision
14	70	L	24	Previous pulmonary tuberculosis, gastrectomy	Bendrofluazide, butazolidine, digoxin, slow K	Nil
15	71	R	64	—	—	Excision
16	76	L	97	Obstructive uropathy	—	Excision

with insulin has previously been described, but of the 3 patients with this condition, one at the time of presentation was satisfactorily controlled by diet alone. The development of gynaecomastia or mammaplasia has not been previously reported after gastrectomy for peptic ulceration, but this was noted in 3 patients.

Many different medications have been associated with gynaecomastia, typically hormones, a variety of tranquillizers (chloropromazine, phenothiozines) and such compounds as spironolactone, amphetamines and digitalis (LeWinn, 1941; Clarke, 1965; Keddie and Morris, 1967; Margolis and Gross, 1967; Ginsburg, 1969; Turkington, 1972). In the present series digoxin had been administered in 5 patients, diuretics in 10 and 2 patients were on steroid preparations. Acetazolamide has not previously been indicated but 2 patients were taking this drug.

Hormones have not been used as a form of treatment in this series as has been advocated (Wernicke, 1939; Buirge et al., 1945), nor local irradication (Gangai et al., 1967; Wolf et al., 1969).

It is difficult to understand why this condition in many patients should be confined to one breast. A local susceptibility has been suggested and trauma has been implicated (Gooel, 1944; Greene and Howard, 1953; Treves, 1958). However, it is probable that trauma may bring the condition to the patient's attention and is not an aetiological factor. In this series no patient gave a history of trauma.

Patients over the age of 25–30 years should be thoroughly investigated and any underlying cause carefully excluded. The incidence of underlying factors is much higher in this series (53 per cent) than in any previously reported.

Acknowledgements

All the patients in this series were under the care of Mr J. Ian Burn and Professor R. B. Welbourn and I am grateful to them for their guidance and encouragement in the preparation of this paper.

References

ASHKAR F. S., SMOAK W. H., GILSON A. J. and MILLER R. (1970) Gynecomastia and mastoplasia in Graves's disease. *Metabolism* **19**, 946–951.

AUGUST G. P., CHANDRA R. and HUNG W. (1972) Prepubertal male gynecomastia. *J. Pediatr.* **80**, 259–263.

BANNAYAN G. A. and HAJDU S. J. (1972) Gynecomastia: clinicopathologic study of 351 cases. *Am. J. Clin. Pathol.* **57**, 431–437.

BECKER K. L., WINNACKER J. L., MATTHEWS M. J. and HIGGINS G. A. (1968) Gynecomastia and hyperthyroidism. An endocrine and histological investigation. *J. Clin. Endocrinol. Metab.* **28**, 277–285.

BUIRGE R. E., SAMUELS L. T. and MCCARTNEY J. S. (1945) Treatment of pubertal bilateral gynecomastia. *Surgery* **17**, 397–403.

CLARKE E. (1965) Spironolactone therapy and gynecomastia. *JAMA* **193**, 163–164.

DEXTER C. J. (1956) Benign enlargement of the male breast. *New. Engl. J. Med.* **254**, 996–997.

FREEMAN R. M., LAWTON R. L. and FEARING M. O. (1968a) Gynecomastia: endocrinilogic complication of haemodialysis. *Ann. Intern. Med.* **69**, 67–72.

FREEMAN R. M., LAWTON R. L. and FEARING M. O. (1968b) Gynaecomastia in renal failure. *Br. Med. J.* **1**, 381–382.

GANGAI M. P., SHOWN T. D., SIEBER P. E. and MOORE C. A. (1967) External irradiation: a successful modality in preventing hormonally induced gynecomastia. *J. Urol.* **97**, 338–339.

GINSBURG J. (1969) Gynaecomastia. *Practitioner* **203**, 166–170.

GOOEL E. F. (1944) Gynecomastia with report of 7 cases. *Surgery* **15**, 938–945.

GREENE W. W. and HOWARD N. J. (1953) Relation of trauma to lesions of male brest. *Am. J. Surg.* **85**, 431–437.

JACOBS E. C. (1948) Gynecomastia following severe starvation. *Ann. Intern. Med.* **28**, 792–797.

KAMINSKY H. H. (1969) Gynecomastia in patients immobilized in Spica casts. *JAMA* **210**, 2395–2396.

KEDDIE N. and MORRIS P. J. (1967) Male breast tumours. *Surg. Gynecol. Obstet.* **124**, 332–336.

LEWINN M. L. (1941) Gynecomastia: hypertrophy of male breast. *J. Clin. Endocrinol. Metab.* **1**, 511–514.

LINDSAY R. M., BRIGGS J. D., LUKE R. C., BOYLE I. T. and KENNEDY A. C. (1967) Gynaecomastia in chronic renal failure. *Br. Med. J.* **4**, 779–780.

MARGOLIS I. B. and GROSS C. G. (1967) Gynecomastia during phenothiazine therapy. *JAMA* **199**, 942–944.

NICOLIS G. L., MODLINGER R. S. and GABRILOVE J. L. (1971) A study of the histopathology of human gynecomastia. *J. Clin. Endocrinol. Metab.* **32**, 173–178.

SCHMITT G. W., SHEHADEH I. and SAWIN C. T. (1968) Transient gynecomastia in chronic renal failure during chronic intermittent hemodialysis. *Ann. Intern. Med.* **69**, 73–79.

TREVES N. (1958) Gynecomastia. *Cancer* **11**, 1083–1102.

TURKINGTON R. W. (1972) Serum prolactin levels in patients with gynecomastia. *J. Clin. Endocrinol. Metab.* **34**, 62–66.

WERNICKE H. O. (1939) Gynecomastia. *Surgery* **5**, 217–225.

WHEELER C. E., CAWLEY E. P., GRAY H. T. and CURTIS A. C. (1953) Occurrence of gynecomastia in conjunction with dermatologic disorders. *Arch. Dermatol. Symp.* **68**, 685–692.

WOLF H., MADSEN P. O. and VERMUND H. (1969) Prevention of oestrogen-induced gynecomastia by external irradiation *J. Urol.* **102**, 607–609.

Br. J. Surg. Vol. 62 (1975) 330–332

Cavernous haemangioma of the frontal bone: case report

S. D. GUPTA, I. N. TIWARI AND N. K. PASUPATHY*

SUMMARY

A rare case of haemangioma of the frontal bone is presented together with a review of the literature. Carotid angiography was found to be a useful diagnostic aid to differentiate it from other lesions of the frontal bone. The best treatment is to excise both tables containing the haemangioma together with a rim of healthy bone in one block.

SKELETAL angiomas localized in a bone occur fairly frequently (Hitzrot, 1917; Anspach, 1937; Sherman and Wildner, 1961), but involvement of the skull bones, especially the frontal bone, is extremely rare. The first descriptions of a vascular tumour of the parietal bone appeared as early as 1845 and 1847 by Toynbee, but the first proved case of frontal bone haemangioma was reported by Mazzini and Brachetto-Brain as late as 1935. Since then very few solitary case reports have been added to the literature (Abbott, 1937; Keleman and Holmes, 1948; Wyke, 1949; Holmes et al., 1952). The present case is being reported because of its rare and interesting features and the pitfalls regarding its clinical diagnosis and management.

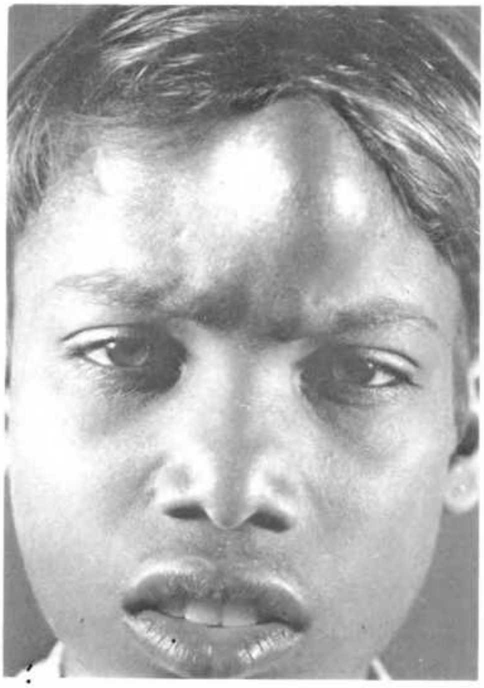


Fig. 1. Preoperative photograph of the patient.

Case report

R. a 13-year-old boy, was admitted to Jawaharlal Institute of Post Graduate Education on 20 March 1973 with the complaint of a gradually increasing painless swelling over the centre of the forehead of 8 years' duration (*Fig.* 1). There was no history of trauma or any symptoms suggestive of increased intracranial tension. On examination there was a hard bony swelling measuring 6 × 4·5 cm situated above the medial half of the right supra-orbital ridge and glabella. The skin over the swelling was normal and freely mobile. A vertical furrow with pulsation was felt over the centre of the swelling. There was a dilated pulsatile vessel running from the right temporal region to the upper part of the swelling. The patient had no neurological deficit. Cerebrospinal fluid findings, fundus examination and haematocrit values were normal.

An anteroposterior X-ray of the skull showed a very clear 'honeycomb' structure. Bony spicules arranged in a 'sun ray' pattern were seen on the lateral view. The outer table was replaced by the growth and the inner table also showed expansion and invasion (*Fig.* 2). A right carotid angiogram showed that the main blood supply of the growth was from a branch of the superficial temporal artery, and in the venous phase the dye was seen to diffuse into the superior sagittal sinus (*Fig.* 3).

At operation (May 1973) a forehead flap was made from one pterion to the other. An area of 2 cm surrounding the swelling was very vascular owing to the presence of many feeding vessels. Six trephine holes were made and interconnected. The inner table was lifted up from the dura mater, through which the feeding vessels emerged and then entered the haemangiomatous mass via the inner table. Both the tables containing the haemangiomatous mass with a rim of healthy bone were removed. The bony defect which measured 6·5 × 8 cm was bridged by split rib grafts. The cut sections of the specimen showed typical perpendicular striations filled with blood (*Fig.* 4).

The postoperative period was uneventful. The pathology report indicated a primary cavernous haemangioma of the bone (*Fig.* 5). The patient was followed up for a period of 6 months. The scar was well healed and the contour of the forehead was well maintained (*Fig.* 6).

Discussion and review of the literature

Though the incidence of skeletal angiomas forms 0·7 per cent and skull angiomas 0·2 per cent of all osseous tumours, frontal bone angiomas are still rarer (Geschickter and Copeland, 1936). Altogether 9 cases of frontal haemangioma have been reported in the literature in the past 100 years (*Table I*). Of the 9, only the last 5 cases have been proved. The lesion was reported as congenital in origin by Abbott (1937) and traumatic by Pilcher (1894), Mazzini and Brachetto-Brain (1935) and Wyke (1949). The present case had no history of trauma, as in the 4 cases reported by Kelemen and Holmes (1948) and Holmes et al. (1952).

There was nothing specific in the clinical findings except that the centre of the tumour was soft and pulsatile, as in those described by Zajaczkowski (1901). Wyke (1949) suggested that the radiological appearance of a 'sun ray' pattern is diagnostic of a haemangioma of the frontal bone as well as the findings of expansion and rarefaction of the bone without reactive

---

* Department of Surgery, Jawaharlal Institute of Post Graduate Medical Education and Research, Pondicherry, South India.

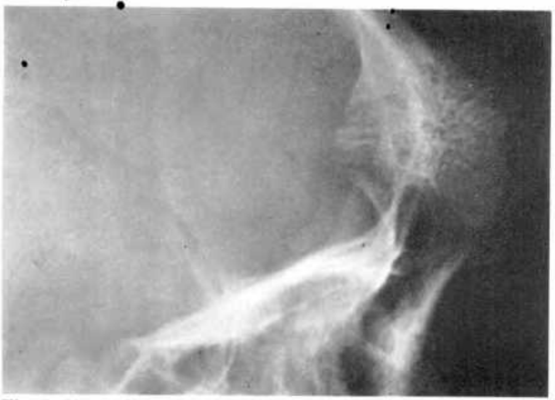


Fig. 2. X-ray film of the skull showing the 'sun ray' pattern of the tumour and expansion of the outer and inner tables.

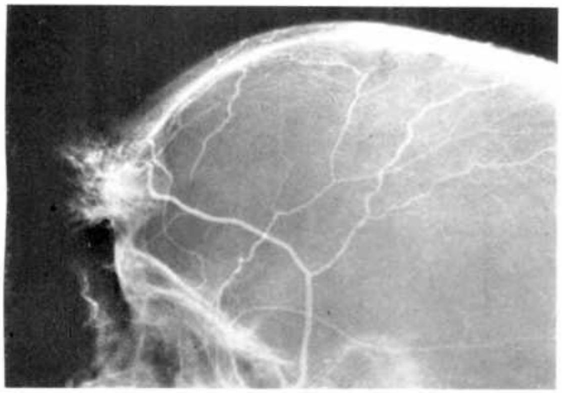


Fig. 3. Carotid angiogram showing a feeding vessel from a branch of the superficial temporal artery.

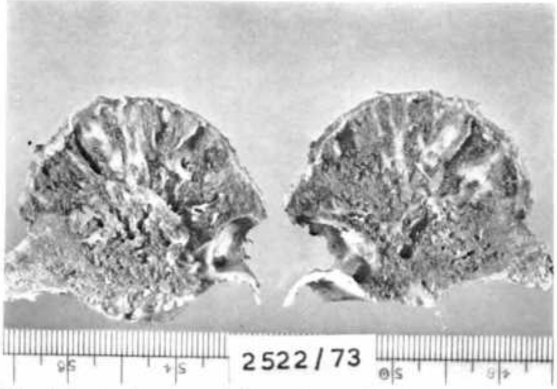


Fig. 4. Sagittal section of the specimen showing perpendicular striations filled with blood.

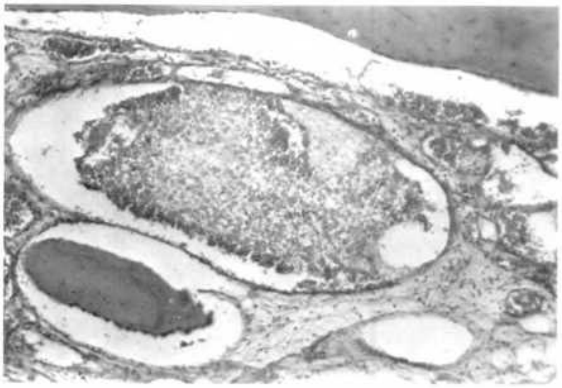


Fig. 5. Photomicrograph showing blood-filled spaces with lamellar pattern.

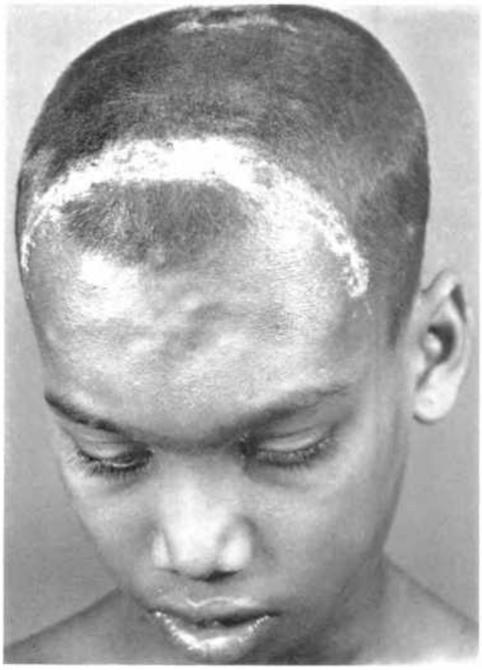


Fig. 6. Postoperative photograph of the patient.

Table I: SUMMARY OF CASES REPORTED IN THE LITERATURE

Author	Age	Sex	Site in skull	Diagnosis	Surgery	Results
Pilcher (1894)	15	F	Frontal	—	Removed piecemeal	Not given
Eros (1928)	70	F	Right and left frontal	—	Died	Died
Mazzini and Brachetto-Brain (1935)	39	F	Right frontal	—	Removed	Not given
Abbott (1937)	3	F	Right frontal	—	Removed	Not given
Keleman and Holmes (1948)	35	M	Frontal	Preop. X-ray, biopsy	Outer table resected	Alive
Wyke (1949)	28	F	Left frontal	Preop. X-ray, biopsy	Both tables resected	Alive
Holmes et al. (1952)	54	F	Right frontal	Preop. X-ray, biopsy	Both tables resected	Alive
	52	F	Right frontal	Preop. X-ray, biopsy	Both tables resected	Alive
	45	F	Right frontal	Preop. X-ray	No surgery done	Alive

sclerosis. In the present case all these features were present except that some reactive sclerosis was also noticed, perhaps because the lesion was of long duration (8 years).

The first case of successful removal with recovery of the patient was reported by Pilcher (1894) who excised the tumour piecemeal. Zajaczkowski (1901) and Keleman and Holmes (1948) experienced problems of haemorrhage during the operation, postoperative meningitis and finally recurrence because they removed the outer table only. Therefore the best treatment is surgical excision of both tables containing the haemangiomatous mass together with a rim of healthy bone.

Acknowledgements

We are grateful to Dr M. Balasubrahmanyan, Principal of Jawaharlal Institute of Post Graduate Medical Education, Pondicherry, for allowing us to publish this paper. Our thanks are due to Dr N. P. Singh, Professor and Head of the Department of Anaesthesiology and Dr A. K. Bhattacharya, Professor of Radiology, for their cooperation in this work.

References

ABBOTT W. D. (1937) Angioma of the skull. *Ann. Surg.* **106**, 1100–1105.

ANSPACH W. E. (1937) Sunray haemangioma of bone with special reference to roentgen signs. *JAMA* **108**, 617–620.

EROS G. (1928) Multiple Haemangioma der Schadelknochen. *Zentralbl. Allg. Pathol.* **43**, 532–538.

GESCHICKTER C. F. and COPELAND M. M. (1936) *Tumours of Bone* (rev. ed.). New York, The American Journal of Cancer.

HITZROT J. M. (1917) Haemangioma cavernosum of bone. *Ann. Surg.* **65**, 476–482.

HOLMES E. M., SWEET W. H. and KELEMEN G. (1952) Haemangiomas of the frontal bone. Report of three cases. *Ann. Otol. Rhinol. Laryngol.* **61**, 45–61.

KELEMAN G. and HOLMES E. M. (1948) Cavernous haemangioma of the frontal bone. *J. Laryngol. Otol.* **72**, 557–563.

MAZZINI O. F. and BRACHETTO-BRAIN D. (1935) Angioma de frontal. Craniectotomia. *Boll. Trab. Soc. Cirurg. Buenos Aires* **19**, 363–369.

PILCHER L. S. (1894) Venous tumour of the diploë. *Trans. Am. Surg. Assoc.* **12**, 283–285.

SHERMAN R. S. and WILDNER D. (1961) The roentgen diagnosis of haemangioma of bone. *Am. J. Roentgenol. Radium Ther.* **86**, 1146–1159.

TOYNBEE J. (1845) An account of two vascular tumours developed in the substance of bone. *Lancet* **2**, 676.

TOYNBEE J. (1847) Aneurism by anastomosis in the substance of the parietal bone. *Lancet* **1**, 230.

WYKE B. D. (1949) Primary haemangioma of the skull. A rare cranial tumour. Review of the literature and report of a case with special reference to the roentgenographic appearances. *Am. J. Roentgenol. Radium Ther.* **61**, 302–316.

ZAJACZKOWSKI A. (1901) Ein Fall von Angioma cavernosum des Stirnbeines. *Przegl. Chir.* **4**.

Br. J. Surg. Vol. 62 (1975) 333–336

Reviews and notices of books

Operating Theatre Technique
Raymond J. Brigden, London. Third edition. 255 × 192 mm. Pp. 698+vii. Illustrated. 1974. Edinburgh: Churchill Livingstone. £12·50.

The Lewin Committee on Operating Departments reported in 1970, and in the past year there has been official action on its recommendation that non-nursing staff should be recruited and trained as skilled theatre technicians and scrub nurses. It is appropriate that this book should now appear in a third edition, ready to act as an indispensable and probably unique guide for those who train for these positions.

The first 280 pages are devoted to the design, equipment and management of operating theatres, to the work which goes on in them before and during operating sessions, and to the design of electrical, sterilizing and anaesthetic equipment. The information is notably up to date, and presented in an admirably clear yet detailed manner. There is a valuable glossary of technical terms.

There are over 500 illustrations, many being specially posed action photographs of high quality. The remaining 280 pages contain detailed lists and photographs of the instruments used in the main operations of general and specialist surgery.

One experienced theatre sister reported that she found this book 'highly readable and most interesting'; it is also good value for money. If kept in the theatre office it will be in constant use, both as reading for students and as a reference book for everyone.

PETER F. JONES

Gastro-entero-pancreatic Endocrine System. A Cell-biological Approach
Edited T. Fujita, Niigata, Japan. 260 × 163 mm. Pp. 195, with 154 illustrations. 1974. Stuttgart: Georg Thieme Verlag. DM.84.

The title of this book extends the view that hormones derived from the intestine and the pancreas form a continuous and overlapping system regulating the physiological functions of the gut. There are 18 chapters, all by Japanese authors, dealing with methods of identifying the specific cells of origin of the hormones and subsequently describing function. The book derives from a symposium held in 1972, and as such suffers from the inevitable lack of continuity. Nevertheless individual chapters are well written, usually with liberal references. Some chapters refer to experiments by the author published elsewhere, and this means that those with a special interest in this field will already be familiar with the results. For those not familiar with the field, the book is a good source of reference but is unlikely to live up to its title in providing a conceptual analysis of an integrated endocrine system.

C. G. CLARK

Pädiatrische Intensivbehandlung
V. von Loewenich and H. Koch. Pp. 142 with 61 illustrations. 1974. Stuttgart: Georg Thieme Verlag. DM.33.

This is a paediatric supplement to a previously published book on intensive care and intensive therapy by P. Lawin. This book discusses resuscitation of the newborn, the place of tracheostomy and long term endotracheal intubation. There are chapters on blood gas analysis and catheterization of the umbilical vessels as well as on oxygen therapy. Prolonged artificial ventilation of the newborn is discussed thoroughly and a special section deals with ventilator treatment in older children. The complications of ventilation treatment are fully discussed.

Prolonged recording of the various parameters of body functions, such as temperature, blood pressure, blood gas analysis etc., are discussed fully. Further chapters deal with acute renal failure and parenteral feeding.

The obvious omissions in this volume are neonatal surgery and the specific problems associated with conditions such as oesophageal atresia, intestinal obstruction and diaphragmatic hernia. It is unfortunate that the authors are working in a paediatric unit which has no direct access to specialized full time neonatal and paediatric surgery.

The book is well produced and contains numerous references but it is unlikely to be of particular interest to surgeons or indeed paediatricians whose knowledge of German is limited.

H. B. ECKSTEIN

Clinical Anesthesia, Monitoring in Anesthesia, Volume 9, Numbers 2 and 3.
Edited William H. L. Dornette. 254 × 175 mm. Pp. 428+xv, with 131 illustrations. 1974. Philadelphia: F. A. Davis Co. (Bristol: John Wright & Sons Ltd). £9·50.

Although there has been an intense interest in monitoring in the past decade it is still true to say that the type of monitoring employed is usually governed by the apparatus available rather than by the clinical importance of the measurement. For example, it is easy to record the ECG but difficult to monitor the cardiac output. Respiratory rate can be determined by many different methods but few instruments are capable of providing continuous and accurate measurements of expired tidal volume.

This unfortunate state of affairs is mirrored in this book. At first sight the list of contents is attractive. The book is divided into four parts dealing with fundamental considerations and pre-, intra- and postoperative monitoring. There are isolated chapters providing a good review of the topic ('safety in the use of monitoring equipment' and 'blood volume studies'), but on the whole the subject matter is descriptive and repetitive. Few authors attempt to define the problem, or to discuss ways in which it might be solved. The result is a multi-author 'cookbook' of monitoring techniques. It may be of some interest to the surgeon who has no previous knowledge of monitoring but it certainly contributes little to the state of the art.

M. K. SYKES

Advances in Surgery. Volume 7, 1973
Edited J. D. Hardy and R. M. Zollinger. 227 × 155 mm. Pp. 277+xiv. Illustrated. 1974. Chicago: Year Book Medical Publishers Inc. (London: Lloyd-Luke Ltd). £11·85.

This latest volume in a well-known series contains sections on the non-operative treatment of solid tumours, the management of colonic polyps, biliary-enteric fistulae, gastro-intestinal haemorrhage, tracheostomy and the surgical treatment of obesity. As would be expected in a volume of this sort, each section is written by experts and is full of information. The largest section is that devoted to gastro-intestinal haemorrhage, which contains a lengthy account of the use of arteriography in the diagnosis of this condition and its treatment by selective arterial infusion of Pitressin; the results reported are impressive, but the reader will look in vain for a balanced appraisal of the contribution of this technique to the problem as a whole, and indeed this whole section suffers from an excess of detail and lack of emphasis. The chapter on biliary-enteric fistulae is a valuable review of a rare condition. The remaining chapters are admirable informative reviews of important aspects of surgery, and in particular that on the surgical treatment of obesity is an excellent balanced discussion of a difficult and controversial subject.

All general surgeons will find something of interest and value in this volume, which should certainly find a place in all medical libraries.

L. P. LE QUESNE

Reviews and notices of books

Review of Medical Microbiology

Ernest Jawtz, San Francisco, Joseph L. Melnick, Houston, and Edward A. Adelberg, New Haven. Eleventh edition. 260 × 180 mm. Pp. 528. Illustrated. 1974. Los Altos, California: Lange Medical Publications. $8.50.

THE new edition of this popular book has been enlarged to include more basic science in order to appeal to medical students as well as to practising clinicians. Those who have long since left the laboratory for the bedside should, if they are interested, have no difficulty in understanding the clear and well-illustrated account of microbial physiology and genetics, mechanisms of immune response and modes of action of antimicrobial agents on microbes. An enormous amount of up-to-date information is to be found, including an account of oncogenic viruses.

The section on antimicrobial chemotherapy is especially useful in simplifying this complex subject and putting new drugs in their appropriate place. The book is dogmatic and without references to published work, but its contents would, in the reviewer's opinion, be accepted with only minor modifications by specialists in the very wide field covered.

For clinicians faced with an unfamiliar infection and little time to read about it, this book would give quick and reliable information.

E. J. STOKES

Arthroplasty of the Hip

Edited George Chapchal. 240 × 170 mm. Pp. 273+x, with 340 illustrations. 1974. Stuttgart: Georg Thieme Verlag. DM.78.

IN recent years there has been an increasing tendency for international surgical meetings to concentrate on a single theme. This volume shows how rewarding this can be. It is an edited report of the proceedings of the fifth international symposium on special orthopaedic themes organized in Holland. This symposium on arthroplasty of the hip was attended by surgeons from twenty-two countries. The participants are to be congratulated for having given as much time to consider the errors and problems of hip arthroplasty as to the successes achieved.

The proceedings have been edited into four sections: the first is concerned with biomechanical problems and the use of acrylic cement in total joint replacement; the second with the indications and contra-indications of various techniques of hip arthroplasty; the third section deals with difficulties and errors and the closing chapter the successes and failures. The symposium represents an excellent survey of the present state of our knowledge about arthroplasty of the hip joint on an international basis.

The volume is elegantly produced with clear diagrams and radiographs. British readers will especially thank the editor for having produced this volume in excellent English from papers which were no doubt originally given in half a dozen or more languages. We may anticipate with pleasure the further publication of the proceedings of subsequent international specialist meetings organized by our Dutch colleagues.

L. KESSEL

The Esophagus

Edited W. Spencer Payne and Arthur M. Olsen, Rochester, Minnesota. 240 × 160 mm. Pp. 339+xvi. Illustrated. 1974. Philadelphia: Lea & Febiger (London: Henry Kimpton). £7·60.

THE editors and the fourteen contributors of this book are all members of the staff of the Mayo Clinic and this book is a 'review of the Mayo Clinic experience with the esophagus and conditions affecting it'.

In order to prepare 'a relatively brief, readable yet comprehensive book' the editors state that they have tried to limit the bibliography. This has been achieved rather unevenly, and some chapters would benefit by the inclusion of reference to earlier workers. An account of the difficulties met with by the pioneers often makes it easier to understand the reason for adopting certain principles in management which are accepted today. This is, however, a very minor criticism. The whole layout of the book is excellent and the text and the illustrations are clear and helpful.

The anatomy and function of the oesophagus are described in a masterly way.

The diagnostic techniques are considered under three headings, 'Radiologic, Endoscopic and Physiologic'. A very clear evaluation is made of each particular method and this section is very helpful.

The techniques of oesophageal dilatation are discussed in detail, and great value is attached to the preliminary swallowing of a guide thread in suitable cases, the management of the chronic corrosive stricture by frequent bouginage using a guide thread is described and the occasional indications for surgical intervention are considered. The management appears to be very similar in principle to the 'auto-bouginage' advocated by Grey Turner and which has proved a safe and satisfactory treatment for many corrosive strictures.

The problem of reflux oesophagitis and hiatal hernia is described well and the management advocated is sound. It is refreshing to see conservative measures recommended in patients with a sliding hernia and with minimal symptoms. The less common para-oesophageal hernia always presents a potential hazard and operation should be considered in most cases. As regards the sliding hernia which requires operative treatment the value of Nissen's fundoplication is recognized.

Carcinoma of the oesophagus is discussed and the various methods of reconstruction are described. The editors, like the reviewer, conclude that in the majority of cases the 'stomach furnishes the quickest, easiest and safest method of reconstruction'.

All in all, this is a first class monograph in which the editors have managed to assemble a large amount of wise advice in a clear and readable manner. It should be read by all surgeons who practise oesophageal surgery.

R. H. FRANKLIN

Surgery of the Liver and Portal Circulation

William V. McDermott, Boston. 260 × 185 mm. Pp. 190+ix. Illustrated. 1974. London: Henry Kimpton. £6·65.

DR McDERMOTT is an international authority on liver surgery and particularly the surgery of portal hypertension. In setting out to produce a concise but comprehensive account of the subject he accepted a challenge which has frequently defeated the expert. In the event he has succeeded admirably. The book is beautifully written with excellent diagrams that enable the reader to follow with ease the investigations and treatments currently in use. The bibliography is well chosen and arranged in such a way that reference can be made quickly to classic articles or the subject can be explored in depth. There is just enough data in the chapter on liver transplantation for the postgraduate student in training or the general surgeon who wishes to remain informed. The book is excellently produced and can be recommended wholeheartedly to libraries or surgeons who want a concise but authoritative account of the present status of liver surgery.

J. H. PEACOCK

Surgery

R. M. Kirk, Willesden General Hospital, J. Maynard, London, and A. N. Henry, London. 250 × 195 mm. Pp. 384. Illustrated. 1974. Tunbridge Wells: Pitman Medical. Cased £5·50 (supplied); paperback £3·50.

THIS is a surgical textbook for the undergraduate student at the beginning of his studies. The book is written in a brief, easily understood manner. It contains sufficient information to enable the student to pass the qualifying examinations in surgery. The presentation of the subject is dogmatic, with the omission in most instances of alternative or controversial views. For this reason the book will be of little help to those working for higher surgical qualifications. The derivation of most medical terms is given, together with short biographical notes on famous people mentioned in the text. These add interest and colour to an otherwise rather dull presentation of the subject. Numerous clear line diagrams are used throughout which certainly help towards a full understanding of the brief text.

The book can be recommended to the undergraduate student.

A. B. BIRT

Current Medical Diagnosis and Treatment

Marcus A. Krupp and Milton J. Chatton, California. 260 × 180 mm. Pp. 1018 + xiv. 1974. Los Altos, California: Lange Medical Publications. £6·25.

THIS book is intended for the practising physician and not as a textbook of medicine. The chapters sometimes achieve this differentiation by tackling organ systems (e.g. the skin, the eye) from the point of view of symptoms, common causes and the approach to treatment. Other chapters are more formal in their approach (breast disease, nutrition). The difficulty with this arrangement is that in trying to provide a ready source of reference on diagnosis and treatment it succeeds in condensing a textbook of medicine and a textbook of therapeutics into a single (though sizeable) volume which may not provide sufficient detail for those who wish to consult it. There is much to be recommended in its therapeutic approach with the kind of advice on such topics as diet, care of the ischaemic foot and the treatment of haemorrhoids which is sometimes hard to find in general textbooks. The essentially didactic approach may well recommend such a book to students, but practitioners treating patients are likely to require much more information in dealing with specific problems.

There is little of surgical interest in this text, as is indicated by the title. Any book dealing 'primarily with internal medical disorders' can hardly discuss the surgical contribution to such disorders if the practising physician is to be sufficiently informed to advise his patients.

C. G. CLARK

Scientific Foundations of Surgery

Edited Charles Wells, James Kyle and J. Englebert Dunphy. Second edition. 278 × 215 mm. Pp. 838 + xix. Illustrated. 1974. London: William Heinemann. £15·50.

WHEN first published in 1967 the *Scientific Foundations of Surgery* was an ambitious concept and was very properly acclaimed. Unlike monographs, a standard work in medicine today—and at its inception this book bid fair to become so—has to provide a continuum of information. Seven years later we see the next stage in its growth; the editors, now with the welcome addition of Professor Dunphy, realize this responsibility, for the new edition is not a simple updating of previous material. The basis of the book has moved further towards science without prejudice to surgery, thus reflecting the very considerable change which has taken place in medicine in the past 7 years. Medicine is what this book is really about; those who read it will be ever more conscious that there are virtually no distinctions left between medicine and surgery—moreover this work is further proof that surgeons are very aware of this fact.

It would be tedious to categorize the realignment of chapters undertaken to bring about this change or the additional material; as would be expected, immunology has won a considerable place—just one example. The total number of contributors has changed very little. Nevertheless of approximately 130 names about half are newcomers; all are men of national and international repute, mostly from the United Kingdom and United States, with some from elsewhere. They have provided a substantial work in which the editors may rightly take pride.

BRYAN N. BROOKE

Basic Gastro-enterology

J. M. Naish and A. E. Read, Bristol. Second edition. 150 × 230 mm. Pp. 480, with 120 illustrations. 1974. Bristol: John Wright & Sons Ltd. £7·50.

THIS is a revised edition of a popular text. Though directed to gastro-enterologists as a primary text, the book appeals to undergraduates, for it is presented in a crisp, readable and easily assimilable style. It achieves its object of providing a sound basic text in an ever-expanding subject. The diagrams are particularly good, and also to be commended are the tables illustrating points in differential diagnosis.

Few textbooks qualify for a place in the personal library, but this one does, both for the teacher and the pupil.

C. G. CLARK

Essentials of Urology

D. E. Sturdy, Newport. 241 × 162 mm. Pp. 306 + vii, with 215 illustrations. 1974. Bristol: John Wright & Sons Ltd. £5·50.

THIS book was written by a general surgeon with a special interest in urology primarily for medical students, but perhaps it will also prove suitable for nurses or for FRCS candidates wishing to revise.

Previously the medical student could study either shorter sections on urology in surgical textbooks written by surgeons with no interest in urology or authoritative tomes in one or more volumes written by surgeons with perhaps too much interest in urology for the average medical student.

This book is concise, clear and well laid out. It is liberally illustrated with line drawings and radiographs.

The text gives a good comprehensive picture of the subject without going into too much detail or contentious argument. Perhaps at times it is too inaccurate; the classification of bladder tumours, for example, which should be accurate is not. Occasionally it is too accurate; total cystectomy, for example, is removal of the bladder but not the urethra or prostate. In general, however, the text is correct, up to date and easily understood.

The line drawings are excellent. There can be no better way of illustrating such a book. With the most minor exceptions—drawings of pyeloplasty copied from other textbooks instead of from the original descriptions, and a drawing of a ureter surmounted by a minute kidney depicting renal agenesis—all the drawings are extremely accurate. The radiographs, which never demonstrate as much when printed as they did on the viewing box, have been well chosen.

Undoubtedly this book fills a gap in the medical literature and, as such, will be welcomed by the medical student.

PHILIP CLARK

Chirurgie der Gegenwart

Edited R. Zenker, München, F. Deucher, Aarau, and W. Schink, Köln. 260 × 180 mm. Vol. 1, pp. 18, 14, 16 and 32. Vol. 4, pp. 51. Illustrated. 1974. München: Urban & Schwarzenberg. No price given.

FURTHER chapters have now appeared for this new multi-volume loose-leaf textbook on general surgery. A chapter by Gierhake on asepsis provides some useful basic information which all surgeons should know about. Other chapters deal with coagulation defects and the use of isotopes in diagnosis, and there is an extensive chapter by Carstensen on electrolyte disturbances. Other subjects dealt with include injuries to the vertebral column, surgery of the liver, reflux oesophagitis and other abdominal conditions.

All the chapters have an up-to-date list of references, and it would appear that once this work is completed it will become the major reference book in general surgery in the German language.

H. B. ECKSTEIN

The Doctor's Lawyer. A Legal Handbook for Doctors

Marc J. Lane, Chicago. 280 × 210 mm. Pp. 99 + xi. 1974. Springfield, Ill.: Charles C. Thomas. No price given.

THIS book, as the subtitle states, is a legal handbook for doctors. It is written by an American lawyer and most of the contents are only applicable to practice in that country. The tax laws are much more the province of the lawyer than the accountant in the United States and the author devotes a considerable part of the book to advice about obtaining maximum tax relief in one form or another. There are also sections on the legal aspects of medical partnership, profit-sharing pension schemes, and life and other insurance.

The only advice applicable to the British doctor is that on avoiding malpractice litigation. This is sound, clear and concise, and is written, like the rest of the book, in a racy style which is pleasant to read. Perhaps a second edition could have a British co-author, in which case the handbook would be very useful.

BERNARD LUCAS

Reviews and notices of books

Die vaginalen Operationen

Gunther Reiffenstuhl, Salzburg, and Werner Platzer, Innsbruck. 278 × 212 mm. Pp. 732 + xi, with 371 illustrations. 1974. Berlin: Urban & Schwarzenberg. No price given.

THIS atlas of vaginal surgery is the culmination of a combined effort by an anatomist, a gynaecologist and one of Austria's outstanding medical artists. The first section of the volume is devoted to the anatomy of the female genital tract and is illustrated by a series of exceedingly clear colour drawings which in themselves should be of great interest to all anatomists.

The majority of the volume is devoted to the various standard vaginal procedures which are performed in gynaecology, and these are described in great detail, not only in words but also with the same clear colour drawings. Each section draws particular attention to the pitfalls and mistakes which can be made and suggests how these can be avoided.

The authors do not attempt to evaluate the relative values of vaginal as contrasted to abdominal approaches to various conditions but aim simply to set out in detail the operative technique of the various vaginal procedures. There is no doubt whatever that this will become the standard work on vaginal surgery, and because of the clarity of many illustrations an extensive knowledge of German is not necessary to follow the context of this book. In view of the obvious cost of producing such a large number of really first class illustrations, one hopes that the publishers will decide to have the text translated into English so as to increase the potential readership considerably.

No price has been quoted for this volume, but in view of the standard of printing and reproduction the price is likely to be very high. In spite of this, the reviewer (who is no gynaecologist) feels certain that this volume is an unqualified success.

H. B. ECKSTEIN

Diseases of the Knee Joint

I. S. Smillie, Perthshire. 245 × 190 mm. Pp. 459. Illustrated. 1974. Edinburgh: Churchill Livingstone. £16.

HAVING read and respected Professor Smillie's classic on injuries of the knee for many years, one was eager to see how he had dealt with the numerous non-traumatic conditions which he must have seen. This contribution appears to be a combined textbook, monograph and patient vignettes, the latter being rather too frequent and detracting from the otherwise excellent observations. The reviewer was depressed to see such terms as 'patella alta', or even 'patella baja' being introduced into the world literature again. The chapter headings and divisions into such subjects as synovial affections, general or local etc., seemed rather unusual and restrictive. The pathological description of rheumatoid arthritis and haemophilla suggested that the author had not carried out this type of work in a 'combined clinic' setting. Quotations from other people's work in these fields were misleading and very few would accept their value, e.g. never use a tourniquet in haemophilla surgery, or Kessel's forage for Blount's disease or even the author's own technique of using Teflon membrane as an interposition barrier to limit adhesion formation after synovectomy.

However, the real mastery and authority appear in the chapters on osteochondritis diseases and on the amazing number of pathologies producing angular deformities around the knee at various ages, with their surgical correction. The illustrations are numerous and colourful and make this publication quite unique. Finally, the literature search has been extensive and industrious and for this reason alone this book is worth its place in a departmental library or on the book shelves of experienced orthopaedic surgeons.

R. B. DUTHIE

Book notices

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and those having the greatest interest to our readers]

National Institutes of Health. Statistical Reference Book of International Activities Fiscal Year 1973
Prepared by International Co-operation and Geographic Studies Branch, Fogarty International Center. 110 × 190 mm. Pp. 52 + vi. 1974. Maryland: Department of Health, Education and Welfare. No price given.

Electrocardiograms: A Systematic Method of Reading Them
Michael L. Armstrong, Sydney. Third edition. 250 × 175 mm. Pp. 80, with 88 illustrations. 1974. Bristol: John Wright & Sons Ltd. £2.

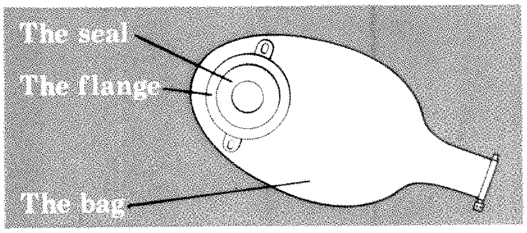
Benign Enlargement of the Prostate
K. E. D. Shuttleworth, R. W. Lloyd-Davies and Raymond Greene. 210 × 140 mm. Pp. 120 + vii, with 89 illustrations. 1974. London: William Heinemann. £4.

Environmental Health Perspectives. Experimental Issue No. 7 May 1974. Low Level Lead Toxicity and the Environmental Impact of Cadmium
260 × 195 mm. Pp. 323 + iv. Illustrated. 1974. Maryland: Department of Health, Education and Welfare. $12.15 p.a.

The continuing story of your successful ostomy

Good reasons why REDIFIT is the ostomy appliance for your patient.

Redifit will give added comfort and confidence to the Ostomist because it incorporates the following distinct advantages:



THE SEAL
The seal is of a superior Karaya gum which will not cause any irritation to the most sensitive skin. It will not distort, and will always create a perfect seal with the skin. It is less affected by extremes of temperature and humidity and so will always come to you in perfect condition.

THE FLANGE
This is a new pattern, unique to Redifit. It is not fastened directly to the bag but is held by a collar on which it can rotate. Therefore even after the bag is fixed in position, the angle of the flange can be adjusted to give the most comfortable position for the belt.

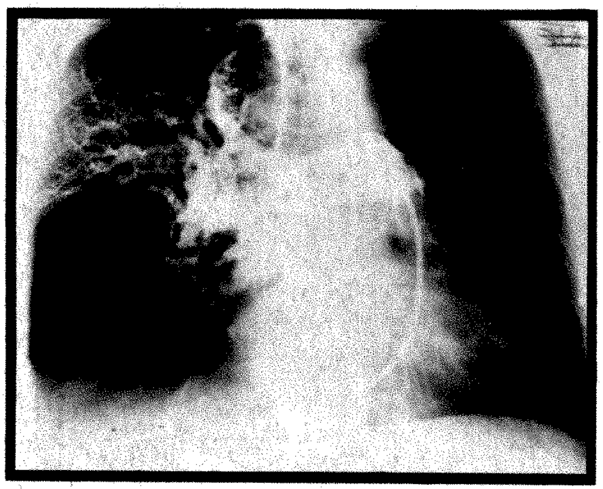
THE BAG
Redifit bag has no less than five laminations of plastic, and is guaranteed odour-proof for the normal life of the bag.
With only one layer of film, one cannot be sure of avoiding the embarrassment of escaping odour.

COMPETITIVE COST

Redifit for the special needs of special people

Downs Surgical Ltd
CHURCH PATH, MITCHAM, SURREY 01-648 6291

RED
ALERT!



When acute massive pulmonary embolism occurs put them on Kabikinase to dissolve the embolus and the still threatening deep vein thrombus and restore the flow. (Lysis achieved, anticoagulate with heparin to prevent rethrombosis.)
"We believe that the current treatment of choice for most cases of acute life-threatening pulmonary embolism is streptokinase." 1
1 Comparison by Controlled Clinical Trial of Streptokinase and Heparin in Treatment of Life-threatening Pulmonary Embolism. Brit. med. J. **1.** 343 (1974).

KABIKINASE

(pure streptokinase)

Full information, brochure and wall card on request.

Kabikinase is manufactured by AB Kabi, Stockholm, Sweden, and is available only from:

KabiVitrum Ltd
Bilton House, Uxbridge Road,
Ealing, London W5 2TH.
Telephone: 01-567 4717 01-579 1871

P.L. No. 0022/5006
Kabikinase is a registered trade mark.

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU

Trasylol

significantly reduces mortality and morbidity in acute pancreatitis

Trapnell, J. E. *et al.* (1974) *British Journal of Surgery*, **61**, 177.

Trasylol®

(aprotinin)

Bayer BAYER

® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

Vol. 62 : No. 5 : May 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

*A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society)
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
I. D. A. JOHNSTON Newcastle
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN McADAM Kampala : Uganda
A. C. McEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX
Subscription £15 per annum, post free. Single copies £1·50, post free

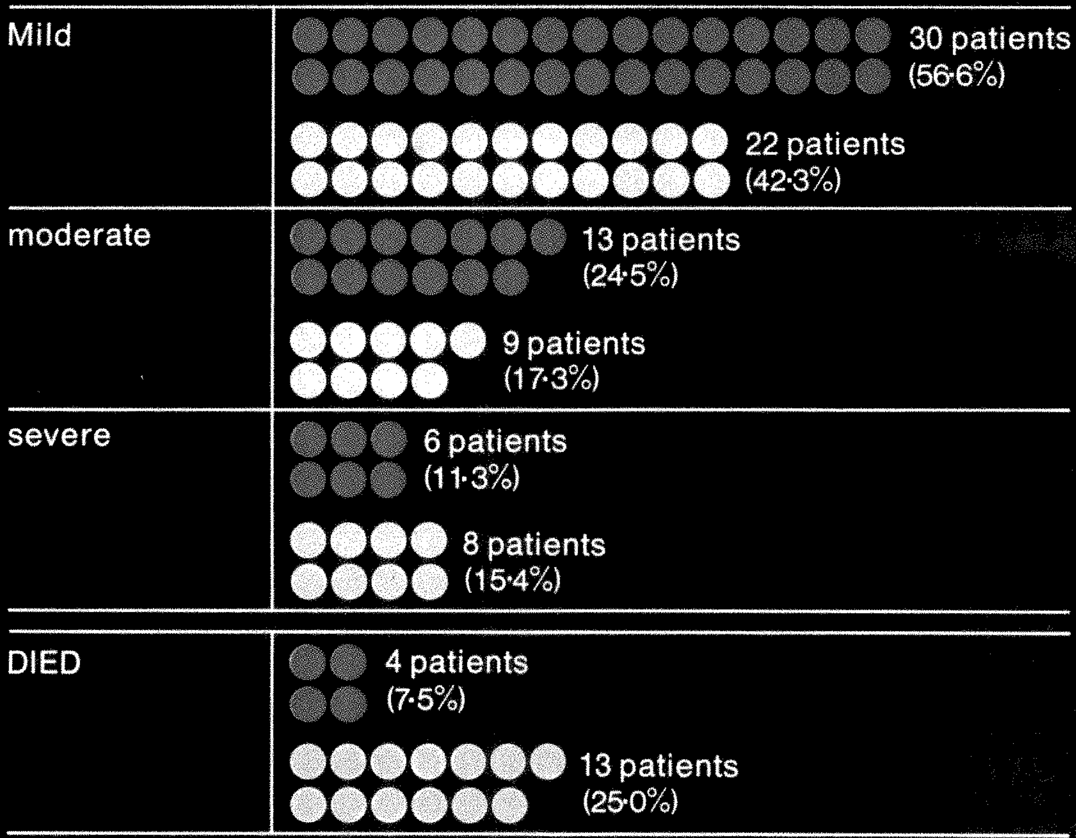
---

THE WILLIAMS & WILKINS CO., BALTIMORE
Subscription $36·00 per annum. Single copies $3·00
Second Class Postage paid at Baltimore, and at additional mailing offices.

The new evidence for Trasylol in the treatment of acute pancreatitis

Course of illness

Prospective double-blind trial in 105 patients over a five year period shows Trasylol to significantly reduce mortality and morbidity in acute pancreatitis.[1]



● Trasylol group (53)
○ placebo group (52)

'Trasylol must therefore be regarded as a drug which is beneficial in the treatment of acute pancreatitis.'[1]

[1] Trapnell, J.E. *et al.* (1974) *British Journal of Surgery*, **61**, 177

Trasylol®

(aprotinin)

Bayer

® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

The British Journal of Surgery

Vol. 62 : No. 5 : May 1975

Original papers

		Page
Intra-arterial infusion of Solcoseryl: a clinical trial of a method of treatment for pre-gangrene of the lower limb	D. Charlesworth, P. L. Harris and M. K. Palmer	337
Extended deep femoral angioplasty: an alternative to femoropopliteal bypass	L. T. Cotton and V. C. Roberts	340
Hydronephrosis complicating aortic reconstruction	Gordon Heard and Graham Hinde	344
Small doses of subcutaneous sodium heparin in the prevention of deep vein thrombosis after elective hip operations	Venous Thrombosis Clinical Study Group	348
The construction of a skin-lined hemithorax in pigs	Lade Wosornu	351
Postvagotomy dysphagia	J. D. Spencer	354
The relationship of anaemia to gastric secretion more than 15 years after vagotomy and gastro-enterostomy	E. J. Wheldon, C. W. Venables and Ivan D. A. Johnston	356
Pancreatic pseudocysts in children: 4 cases from Uganda	J. Wilson Carswell, J. Cotter and S. P. Master	360
Diagnosis, clinical course and treatment of acute dermal gangrene	I. McA. Ledingham and M. A. Tehrani	364
Gas gangrene of the extremity: the presenting clinical picture in perforating carcinoma of the caecum	R. Mzabi, H. S. Himal and L. D. MacLean	373
Wound infections due to *Bacteroides fragilis* following intestinal surgery	D. A. Leigh	375
Pneumatosis cystoides intestinalis with unexplained ascites in Ethiopian patients	Edemariam Tsega	379
Caecal rupture due to colonic ileus	Eugene D. Gierson, F. Kristian Storm, William Shaw and Susan K. Coyne	383
Epidermoid cysts, polyposis coli and Gardner's syndrome	Barbara Leppard and H. J. R. Bussey	387
Chronic hydradenitis suppurativa: a report of 9 cases	Humphrey Pigott and Harold Ellis	394
Bilateral extradural haematomas	M. V. Subrahmanian, G. B. Rajendraprasad and B. Dibbala Rao	397
Injury of the facial nerve during surgery of the parotid gland	C. M. Ward	401
Recognition of infection associated with intravenous catheters	R. Freeman and B. King	404
Pilonidal sinus treated by phenol injection	B. A. Shorey	407
The surgical management of ingrowing toenail	W. R. Murray and B. S. Bedi	409
Hanging bladder stone formed around Mersilene mesh	P. P. Dongaonkar	413

Reviews and notices of books 415

© John Wright & Sons Ltd and the respective contributors named above, 1975.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any other form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.

SEPTRIN contains trimethoprim
and sulphamethoxazole.
Full prescribing information
is available on request.

References
1. *Med J Aust.* (1973),
Special Suppl., **1**, 58.
2. *Practitioner* (1972), **209**, 838.

Wellcome Medical Division,
The Wellcome Foundation Ltd.,
Berkhamsted, Herts.

Wellcome

Sounds right for Septrin

b.d. in chest infections

Why run the risk of a bacterial chest infection becoming chronic? Experience increasingly indicates the need for prompt, vigorous treatment. Whenever chest sounds indicate infection, rely on SEPTRIN:

- more effective than ampicillin or tetracycline[1,2]
- over 30 million treatment courses prescribed worldwide.

SEPTRIN

TRADE MARK

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 60. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISEMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are two or more authors (apart from the main author), these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title

of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated.

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature* (*Lond.*) **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea **4**, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th 3d. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology.* London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BLAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

Congress Proceedings

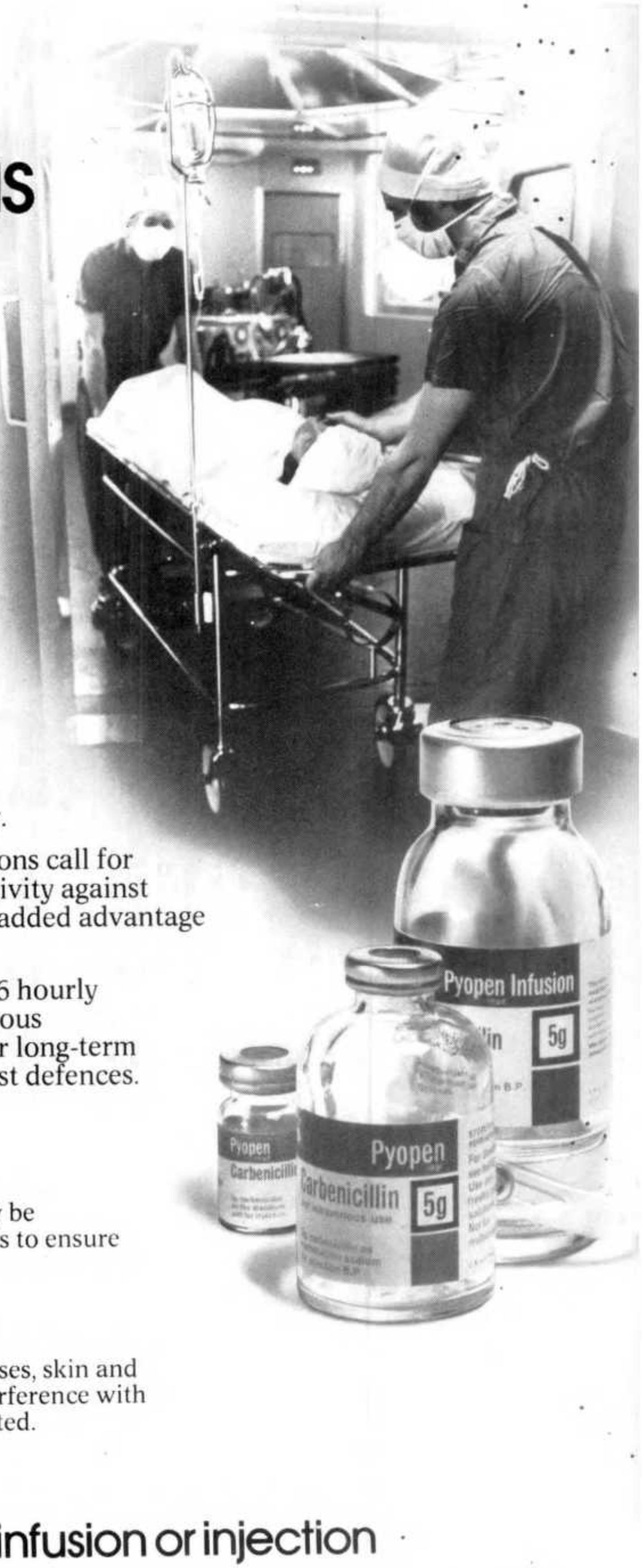
CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding, or that following.

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)

When pseudomonas threatens...



Pyopen

The skill of the surgical team,
hours in the theatre, the most advanced
techniques in the world . . . and infection
can still throw the outcome into jeopardy.

Systemic pseudomonas or proteus infections call for Pyopen. Only Pyopen offers you good activity against these Gram-negative organisms with the added advantage of penicillin safety.

Intravenous Pyopen, at a dosage of 5g 4–6 hourly will rapidly control many of these dangerous infections. And Pyopen is also suitable for long-term therapy and for patients with lowered host defences.

Adult Dosage
5g I.V. 4–6 hourly.
In patients with renal impairment dosage may be reduced; monitoring is advisable in these cases to ensure adequate serum antibiotic levels.
Contra-indication
Penicillin hypersensitivity.
Side-effects
As with other injectable penicillins. In rare cases, skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Pyopen–by infusion or injection

Further information is available on request.
Pyopen* (carbenicillin sodium B.P.) is a British product originated by
Beecham Research Laboratories, Brentford, England. *regd.

Our piggy bank could save your skin

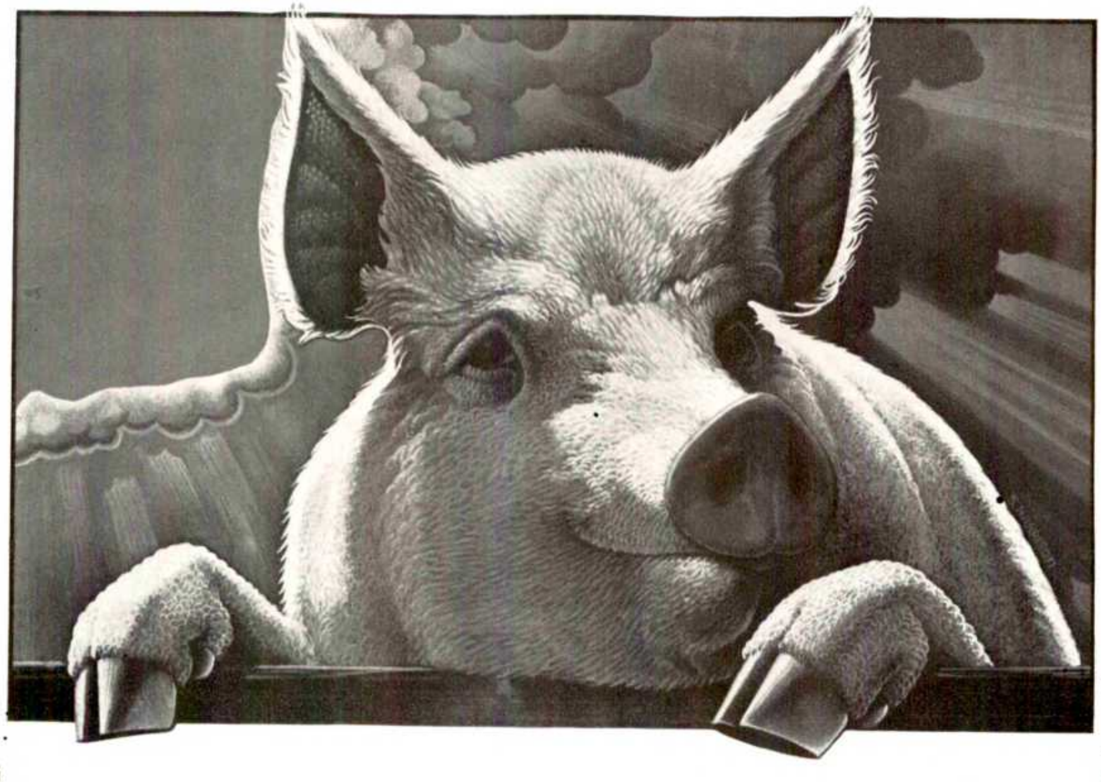
Our Biological Skin Bank provides porcine skin dressings that have many advantages in the treatment of burns, traumatic skin loss, injuries, and soft tissue defects.

These temporary biological dressings dramatically reduce pain, inhibit infection, and reduce fluid and heat losses from the body. They protect exposed tendons, nerves and vessels and aid speedier recovery by allowing increased mobility; by promoting healing, and by improved formation of natural scarring.

The ready availability of the lyophilised Armour porcine skin dressings avoids the problems of obtaining homografts and now gives you an important new weapon in your efforts to provide a more rapid and satisfactory recovery for your patients.

Full information on request
Armour Pharmaceutical Company Limited
Eastbourne, Sussex, England ,BN22 9AG

JA23/ABD/5



ACM endoscopes leave nothing to the imagination

Most surgeons today recognise the superiority of endoscopy as a means of confirming diagnoses of colon diseases. It can be quicker and easier than laparotomy, and is also less traumatic for patients and makes fewer demands on hospital facilities.

The premier instrument for colonic investigations is the ACM F9L coloscope. Advanced features include 12X magnification and a sharp, wide angle circular image three times larger than competitive instrument's.

With it a surgeon can clearly view as far as the caecum, take biopsy specimens and perform polypectomies. After surprisingly little practice, coloscopy can be most rewarding. And the ACM coloscope is exceptionally easy to use – a single, one-handed joystick controls the poly-directional tip.

There's a shorter version, too, the F9S which will reach to the transverse colon and beyond. For the experienced coloscopist there's the dual channel F9A, a major operative, as well as diagnostic instrument.

To find out more, please use the coupon. Or write or telephone.

Please tell me more about ACM endoscopes.
I would like literature only ______ ☐
Please arrange a visit
My telephone number is ______ ☐
Name ______
Address ______
______
______ B.J.S 5-75

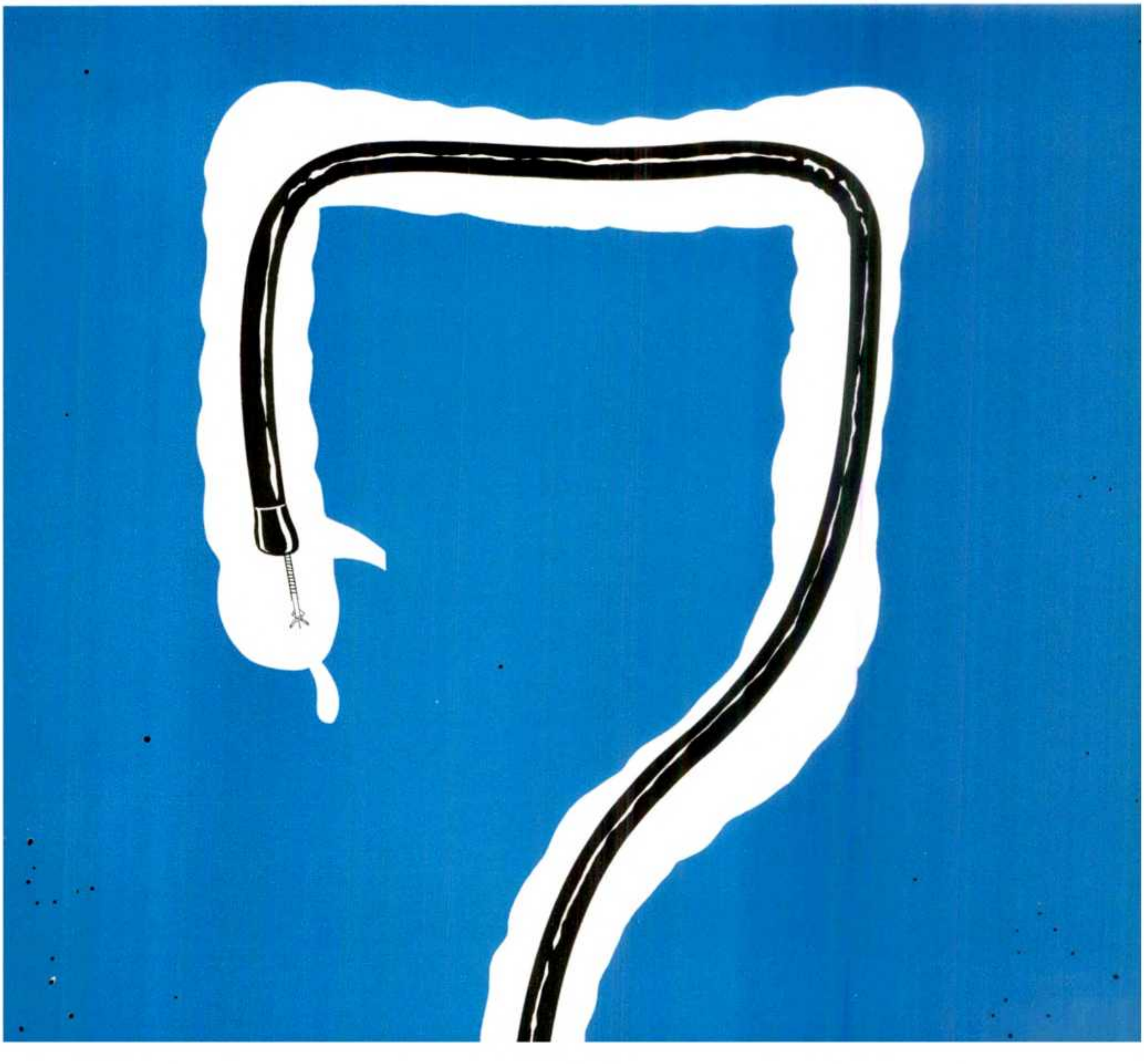
ACM Endoscopes – clearly the best

ACM

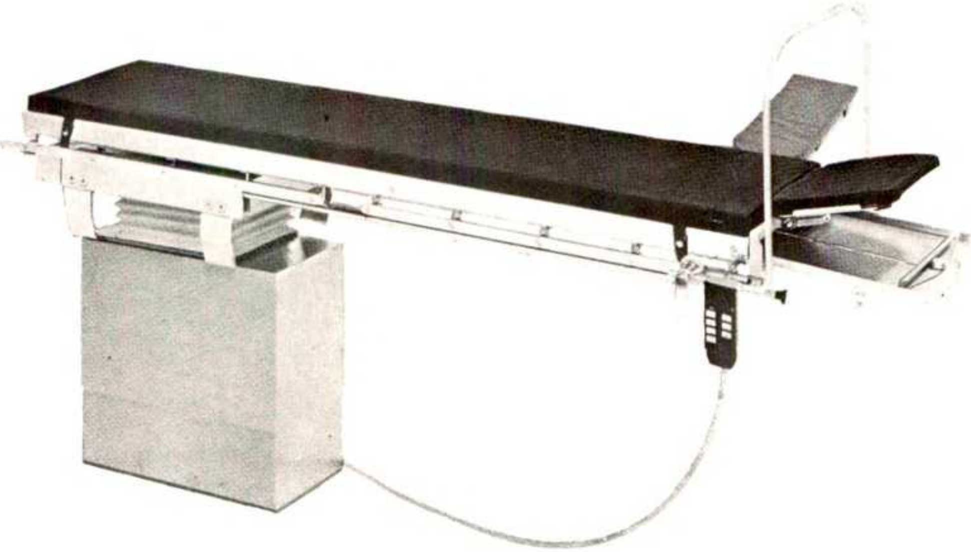
Wappler Endoscopy Limited,
Park House, 22 Park Street, Croydon, Surrey, CRO OYH
Telephone: 01-686 4241

WAPPLER Endoscopy Limited

ACM endoscopes for gastro-enterology, bronchoscopy, urology, gynaecology and teaching.



Just 4 bolts and a compressed air line



that's all it takes to install the KIFA H3 Table

- ★ The most advanced operating table system available
- ★ Reduces patient handling
- ★ Provides unequalled x-ray facilities ★ Easily cleaned
- ★ Utterly reliable ★ Quick turn-round of patients

Table tops available for general, urological, gynaecological, orthopaedic and micro-surgery. Sierex will be pleased to supply details on request.

Sierex

Sierex Limited
15/18 Clipstone Street, London, W1P 8AE, 01-580 2464
Branches in *Aberdeen, Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester and Reading.*
Agents in *Belfast, Newcastle and Newport.*

a choice of fibre light source for every situation

TYPE 2150

. . . for the theatre

Solid state for greatest reliability, with infinitely variable light output from two 150 watt quartz halogen lamps. A heat filter is incorporated to reduce cable temperature and increase cable life. Housed in a robust steel case, making a compact unit, the fan is quiet, and lamp changing is a simple matter.

TYPE 175

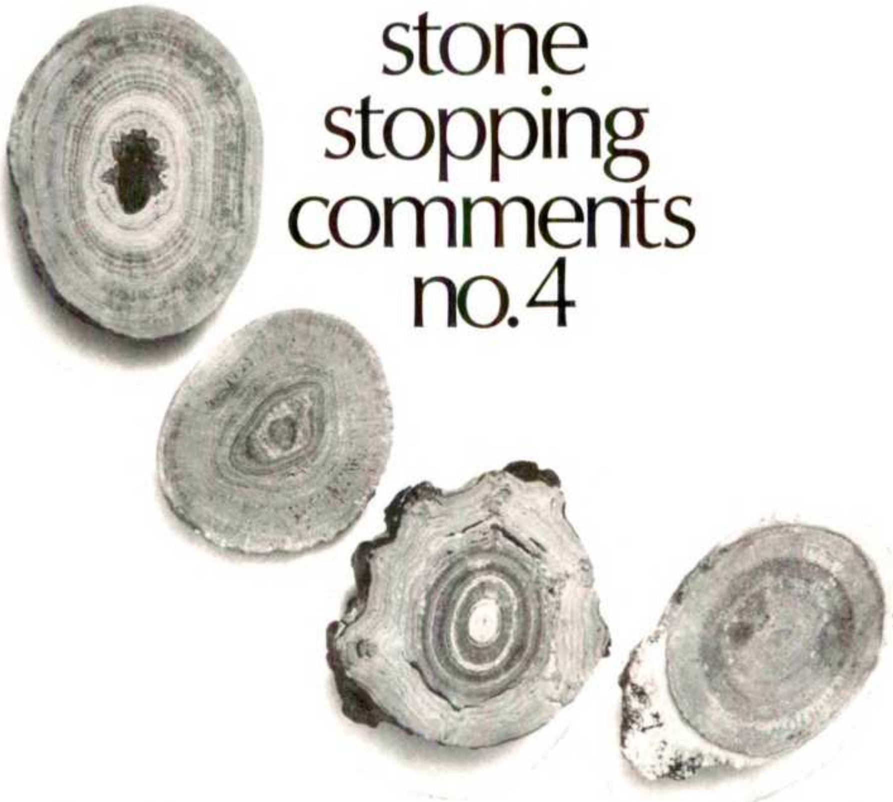
. . . for outpatient Departments

Using a 75 watt high efficiency quartz halogen lamp with di-chroic reflector, the Type 175 incorporates a High/low switch which gives increased lamp life at low settings. Of robust steel construction, the unit occupies very little space, and the fan is quiet in operation.

full specification and details of all fibre light equipment and instruments from

Downs Surgical Ltd

CHURCH PATH, MITCHAM, SURREY Tel 01·640 3422



stone stopping comments no.4

In a recent study[1] measurements of ^{47}calcium and of urinary calcium excretion were made in 125 cases of urolithiasis (78 solitary stone, 47 recurrent).

The authors found that 57 out of 60 patients with hypercalciuria showed raised absorption of ^{47}Ca, whereas 49 out of 106 patients showing similar hyperabsorption of calcium had *normal* calcium excretion. The authors concluded that "…a majority of stone formers, whether they are hypercalciuric or not, absorb calcium excessively from the intestine and this is more prevalent in cases of recurrent urolithiasis."

As a sequel to investigation 1, the same authors[2] studied the effect of Sodium Cellulose Phosphate on intestinal calcium uptake. In comparison to a low calcium, low oxalate diet; "Sodium Cellulose Phosphate can significantly diminish the absorption of calcium from the intestine; there is concomitant diminution of urinary calcium excretion. The plasma levels of the divalent cations do not appear to be influenced by this therapy."

Dosage in this study was varied to evaluate therapeutic effect. "Five grams reduced the intestinal calcium by as much as 85% and even a 1 g dose resulted in a 50% reduction… Such a dose (5 g), however, is probably essential when it is considered that the substance will ordinarily be dispersed throughout a semi-solid food bolus." Optimum administration time was considered to be 5 g t.i.d. at meal times, or within 1 hour after food.

In terms of side-effects and toxicity, the authors stated "Serum levels of calcium and phosphorus were not altered in any of the patients even when the substance had been taken for a period as long as 7 years in a dose of 5 g 3 times daily." There was no diarrhoea or intestinal disturbance, and patients found SCP reasonably palatable and easy to take.

Presentation

Whitish cream powder packaged in paper aluminium polythene single-dose sachets of 5 g each. Supplied in packs of 100.

References

1. Brit J Urol. (1974) **46**: 377-384.
2. Brit J Urol. (1974) **46**: 385-392.

Whatman Sodium Cellulose Phosphate

to reduce dietary calcium absorption.

Full prescribing information is available on request.

Whatman®

Whatman Biochemicals Limited,
Springfield Mill, Maidstone, Kent.
Telephone: Maidstone 61688/9 Telex: 96113

The British Journal of Surgery

Vol. 62 : No. 5 : May 1975

Br. J. Surg. Vol. 62 (1975) 337–339

Intra-arterial infusion of Solcoseryl: a clinical trial of a method of treatment for pre-gangrene of the lower limb

D. CHARLESWORTH, P. L. HARRIS AND M. K. PALMER*

SUMMARY

A randomized double blind trial of the drug Solcoseryl given by intra-arterial infusion was carried out on 57 patients with pre-gangrene of the lower limb. A sequential analysis was carried out and the trial stopped when the results showed a statistically significant result in favour of the active drug.

THE drug Solcoseryl has been shown to accelerate wound healing in rats and to facilitate healing of trophic lesions in patients with arteriosclerosis (Meythaler et al., 1963; Kappert, 1965; Hurlimann, 1970; Malaker and Sellwood, 1970; Kusztos et al., 1972). It is a protein-free extract of calf blood. The analytical data for the extract are known (Jaeger et al., 1965). Solcoseryl has been shown to increase oxygen uptake by liver slices by 200 per cent. It also increases oxygen consumption in substrate-saturated rat liver mitochondria. Its mode of action is not known but it has been suggested that it increases the rate of molecular transport of oxygen, which in turn allows faster rates of flow in capillaries (Dettli, 1973; Laszczower, 1973).

Seventy-five patients with peripheral vascular disease had major amputations of the lower limb at the University Hospital of South Manchester between 1967 and 1971. The average age of the patients was 69 years. One-third of the patients died in hospital following the operation and only a small minority were eventually able to walk on a prosthesis (Harris et al., 1974). The possibility that Solcoseryl might reduce the number of patients who required major amputations of the lower limb obviously merited careful investigation. We therefore carried out a randomized double blind trial of Solcoseryl in 57 elderly patients with pre-gangrene in the leg when the only alternative treatment was amputation.

Patients and methods

Patients with generalized arteriosclerosis who had pre-gangrene in the lower limb were considered for the trial. All the patients had a preliminary aortogram and only the patients for whom it was considered impractical to carry out reconstructive vascular surgery were included. In several patients previous direct arterial surgery had failed to reverse the ischaemic changes. All the patients had undergone a lumbar ganglionectomy on the ipsilateral limb at some stage prior to their inclusion in this trial. There were 57 patients in the trial; 15 were excluded from analysis for various reasons, the majority because the course of treatment was incomplete (*Table I*). Technical difficulties in placing and securing the catheter resulted in most of the failures in the early part of the trial. The average age of the 42 remaining patients was 69·7 years; there were 26 males and 16 females. Treatment was allocated at random by referring to pre-randomized lists; one for the patients with rest pain and the other for diabetics. Solcoseryl was supplied in ampoules, each containing 4 ml. Half the ampoules had red labels and the other half black; one contained the active drug and the other a harmless placebo.

Table I: NUMBER OF PATIENTS EXCLUDED FROM THE TRIAL AND THE REASONS FOR EXCLUSION

Reason for exclusion	Solcoseryl	Placebo
Technical failure	6	6
Adverse reaction	1	0
Intercurrent medical emergency	2	0
Total number excluded	9	6

An infusion of 200 ml of low molecular weight dextran (Dextran 40) was given through a small bore plastic catheter into the common femoral artery on the affected side. A small roller pump (Holter model 212) was used to propel the infusate into the artery and each infusion took approximately 1 hour to complete. Eight ml of the treatment drug were added to the infusate; red label ampoules to one group and black label to the other according to their allocation

---

* University Hospital of South Manchester.

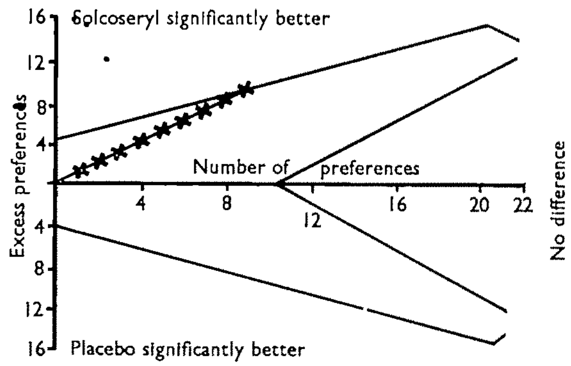


Fig. 1. Sequential analysis chart at a 1 per cent level of statistical significance, showing a significantly better result for Solcoseryl ($P<0{\cdot}01$).

Table II: ARTERIAL LESIONS PRESENT IN EACH GROUP, BASED ON ANGIOGRAMS

Treatment group	Arterial lesion on affected side: Iliac block	SF block	SF stenosis	Tibial block
Solcoseryl	0	16	2	6
Placebo	1	13	2	5
Total	1	29	4	11

SF, Superficial femoral artery.

Table III: NUMBER OF PATIENTS UNDERGOING AN AMPUTATION IN EACH GROUP

Treatment group	Amputation at end of treatment: Yes	No	Total
Solcoseryl	14	9	23
Placebo	19	0	19
Total	33	9	42

Table IV: NUMBER OF PATIENTS IN EACH GROUP IN WHOM THE TREATMENT WAS CONSIDERED SUCCESSFUL

Treatment group	Overall assessment: Success	Failure	Total
Solcoseryl	11	12	23
Placebo	1	18	19
Total	12	30	42

from the pre-randomized lists. The infusion was repeated each day for 10 days.

Treatment was considered to have failed if an amputation was carried out. In the patients who failed to respond to treatment amputation either was demanded by the patient or was suggested by the surgeon and accepted by the patient. The surgeon had no knowledge of whether the patient had been receiving the drug or the placebo. Follow-up of the successful patients was from 6 months to 2 years.

When a pair of patients with rest pain or a pair with diabetes had been treated, one with the active drug and the other with the placebo, their clinical results were made available to the statistician. The conclusion that either Solcoseryl was better or the placebo was better was plotted on a sequential chart by the statistician who was the only person who knew the code. If there was no difference between the responses the results for that pair of patients were ignored in the sequential analysis.

Results

The total number of patients who completed the course of infusions was 42. Thirty-eight patients were matched, giving 19 pairs; in the remaining 4 patients one of the pair failed to complete the course of treatment for technical reasons. Twenty-three patients received the active drug (average age 70·9 years) and 19 patients received the placebo (average age 68·4 years). All the patients had pre-gangrene in one leg. Twenty-eight of the 42 patients had frank gangrene; in the majority it was confined to one or two toes, and the total area of gangrene did not exceed 5 cm^2 in any of the patients. Eighteen patients in the Solcoseryl group had gangrene and 10 patients in the placebo group had gangrene. This disparity is not statistically significant ($\chi^2 = 2{\cdot}09$, $\nu = 1$, $P<0{\cdot}05$).

Nine of the patients in the Solcoseryl group and 9 of those in the placebo group had symptoms in the contralateral limb. The majority of patients had diffuse arteriosclerosis and a complete occlusion of the superficial femoral artery. Six patients in the Solcoseryl group and 5 in the placebo group had arteriographic evidence of occlusions in the tibial vessels (*Table II*). Four patients in each group had clinical evidence of a neurological deficit in the pre-gangrenous limb. The majority of patients had evidence of aorto-iliac disease and a superficial femoral artery occlusion. Both groups were similar in respect to the arterial lesions present.

Eleven of the 23 patients in the Solcoseryl group could walk before treatment began, compared with 11 of the 19 patients in the placebo group. The ratio of diabetic to non-diabetic patients was similar in each group: Solcoseryl, 8 out of 23; placebo, 7 out of 19. Because of the small number of patients the diabetic and non-diabetic patients were not analysed separately.

All the patients in the placebo group had an amputation of some kind (*Table III*). Only 14 patients in the Solcoseryl group had an amputation, and this difference is statistically significant ($P = 0{\cdot}004$, Fisher's exact test). One patient in the placebo group and 2 patients in the Solcoseryl group had a transmetatarsal amputation. All 3 of these patients could walk and were free from pain after an interval of 1 year. In patients who were not diabetic this was considered to be a successful outcome. If we consider the patients who had a local amputation and who were not diabetic as being successes, the figures are: Solcoseryl 11 successes, placebo 1 success, with a total of 30 failures (*Table IV*).

Eleven out of the 23 patients who received Solcoseryl had a result which was considered successful compared with only 1 out of 19 in the placebo group. This difference is statistically significant ($\chi^2 = 7{\cdot}17$, $\nu = 1$, $P<0{\cdot}01$). Patients who were admitted to the trial were also matched according to whether they were diabetic or not, and one of each pair received the active drug, the other the placebo.

Thirty-eight patients were successfully matched, giving 19 pairs, in chronological order of their entry into the trial, but 4 patients, all of whom received Solcoseryl, were without a match. Two of these 4 patients were 'successes' and 2 were 'failures'. In 9 of the 19 pairs the patient receiving Solcoseryl was considered to have fared better than the patient receiving the placebo. In the remaining pairs there was no difference. The probability of all 9 better results being for one treatment is $P = 0{\cdot}004$ (binomial test).

The results were plotted on a sequential chart as they became available (*Fig.* 1). It was decided that the superiority of the active drug would be accepted only if the probability of a positive result occurring by chance alone was less than 0·01. The level of statistical significance was fixed at 1 per cent before the trial began because the treatment was considered likely to be uncomfortable to the patient and to carry a risk of infection.

Discussion

The two groups of patients in this trial were well matched and sequential analysis shows a statistically significant result in favour of Solcoseryl.

There is evidence to suggest that a lumbar sympathectomy done for intermittent claudication does not influence the rate of amputation in patients who subsequently develop pre-gangrene (Bloor, 1961). Most surgeons, however, perform a lumbar sympathectomy in the circumstances we were considering, and approximately half the patients can be expected to improve (Taylor and Calo, 1962; King et al., 1964; Szilagyi, 1967). All the patients in this trial had had a lumbar ganglionectomy on the ipsilateral side at some time before the trial began. Consequently, whatever the mode of action of this drug, it is unlikely to mimic the effects of a lumbar ganglionectomy.

In the placebo control group we infused low molecular weight dextran, which could be expected to improve capillary infusion by reducing viscosity, rather than use a peripheral vasodilator. There is evidence that peripheral vasodilators do not benefit patients with peripheral vascular lesions and there is no reliable evidence to suggest that they do (DeBakey et al., 1947; Coffman and Mannick, 1969; Richards, 1970; Coffman, 1971.)

We concluded that in patients with severe peripheral ischaemia due to arteriosclerosis, Solcoseryl given by the method we describe may help to avoid a major amputation.

Acknowledgments

We wish to thank Dr M. Laszczower of Solco, Basle, for providing the drug and Mr J. Howat and Mr R. Jones for their help with the trial.

References

BLOOR K. (1961) Natural history of arteriosclerosis in the lower extremities. *Ann. R. Coll. Surg. Engl.* **28**, 36–52.

COFFMAN J. D. (1971) The medical management of arteriosclerosis. In: DALE W. A. *Management of Arterial Occlusive Disease.* Chicago, Year Book, pp. 51–62.

COFFMAN J. D. and MANNICK J. A. (1969) Failure of acute vasodilator drug therapy in femoral artery disease at rest and during exercise. *Circulation* **40**, Suppl. 3, 59.

DEBAKEY M. E., BURCH G., RAY T. and OSCHNER A. (1947) The "borrowing-lending" hemodynamic phenomenon (hemometakinesia) and its therapeutic application in peripheral vascular disturbances. *Ann. Surg.* **126**, 850–865.

DETTLI L. (1973) Bemerkungen zum Begriff der perinekrotischen Zone. *Vasa* **2**, 423–424.

HARRIS P. L., READ F., EARDLEY A., CHARLESWORTH D., WAKEFIELD J. and SELLWOOD R. A. (1974) The fate of elderly amputees. *Br. J. Surg.* **61**, 665–668.

HURLIMANN F. (1970) Intra-arterial treatment of peripheral circulatory disorders with trophic lesions. *Praxis* **59**, 1435.

JAEGER K. H., LEYBOLD K., MITTENZWEI H., STAUDINGER H. J. and VON WALDSTATTEN L. (1965) The augmentative effect of a blood extract on cellular respiration. *Drug Res.* **15**, 750–754.

KAPPERT A. (1965) Erfahrungen unit der intra arteriellen Solcoseryl Therapie peripleven Durchblutingsstärungen. *Med. Welt.* **15**, 752–754.

KING R. D., KAISER G. C., LEMPKE R. E. and SCHUMACKER H. B. (1964) Evaluation of lumbar sympathetic denervation. *Arch. Surg.* **88**, 36–46.

KUSZTOS D., BERECZKY M., ABLONCZY D., LANTOS E., LANDI W., WALTON E. and HAJTMAN B. (1972) A controlled trial comparing two drugs used to treat peripheral vascular disorders with trophic lesions. *Vasa* **1**, 212–214.

LASZCZOWER M. (1973) Die perinekrotische Zone. *Vasa* **2**, 421–422.

MALAKER K. and SELLWOOD R. A. (1970) Effect of Solcoseryl on the survival of skin-grafts and healing of donor sites in rats. *Br. J. Surg.* **57**, 221–222.

MEYTHALER F., ELL O. and DERLATH S. (1963) Erfahrungen unit Actihaemyl bei der Behandlung peripleven arteriellen Durchblutingsstärungen. *Munch. Med. Wochenschr.* **105**, 1945–1947.

RICHARDS R. L. (1970) *Peripheral Arterial Disease.* Edinburgh, Churchill Livingstone, p. 63.

SZILAGYI D. E., SMITH R. F., SLERPELLA J. R. and HOFFMAN K. (1967) Lumbar sympathectomy: current role in the treatment of arteriosclerotic occlusive disease. *Arch. Surg.* **95**, 753–759.

TAYLOR G. W. and CALO A. R. (1962) Atherosclerosis of arteries of lower limb. *Br. Med. J.* **1**, 507–510.

Br. J. Surg. Vol. 62 (1975) 340–343

Extended deep femoral angioplasty : an alternative to femoropopliteal bypass

L. T. COTTON AND V. C. ROBERTS*

SUMMARY

The results of extended deep femoral angioplasty (EDFA) have been analysed for 74 legs in 72 patients. In 69 per cent a femoropopliteal bypass would have been possible, so EDFA is considered here as an alternative operation. The success rate was 66·9 per cent, the failure rate 25·6 per cent and no effect was achieved in 7·5 per cent. Diabetes adversely affected the results. Of the failures, 45 per cent were diabetic, while the incidence of diabetes was only 14 per cent in the group where the operation was successful. The long term results of the operation were reasonable, 75 per cent being successful for 10–39 months. Age had no bearing on success or failure.

The effects of EDFA were most dramatic on intermittent claudication. In 52 per cent it was abolished and in 92 per cent claudication distance was increased to over 200 yards. Good results were achieved after failed lumbar sympathectomy and failed femoropopliteal bypass.

Successful results of EDFA could be predicted best by inspection of angiograms. Success or failure could have been predicted from the state of the run-off in 81 per cent of the cases. Claudication and rest pain were the most relieved by EDFA, followed by ischaemic ulceration of the leg. Gangrene of digits was helped but less than had been hoped.

We conclude that the indications for femoropopliteal bypass are limited to cases of digital gangrene where angiography shows that bypass is possible or where an EDFA operation has failed.

In February 1973 we produced a preliminary report on the operation that we described as 'extended deep femoral angioplasty' in a group of 34 patients suffering from claudication, rest pain and gangrene due to atherosclerotic disease sited below the level of the inguinal ligament (Berguer et al., 1973). Credit must be given to Martin et al. (1968) who showed the effectiveness of revascularization of the leg by opening up the orifice of the deep femoral artery. Our contribution, first reported in 1971 (Cotton, 1971) and independently by Martin et al. (1972), has been to show how extension of the angioplasty down to the first, second or third bifurcation of the deep femoral artery is even more effective. It must be stressed that the operation of EDFA means that the deep femoral artery must be mobilized and patched very extensively for as much as 15 cm of the main trunk of the deep femoral artery. In all the 'run-in' was considered satisfactory as judged by a good femoral pulse and a satisfactory filling of the aorta and iliac arteries in aortograms. This present paper analyses our further experience in a total of 74 EDFAs performed over a period of 44 months from April 1970. Before our description of this operation the operation of choice was a femoropopliteal bypass graft using an autogenous vein, the reversed long saphenous vein. EDFA has, in our experience, become the first operation to be tried for most cases of ischaemic disease below the level of the inguinal ligament.

We believe many vascular surgeons, especially in Great Britain, have performed fewer femoropopliteal bypass operations in recent years for a variety of reasons. The operation has an immediate failure rate of at least 3 per cent. At 5 years the patency rate has reduced to 61·5 per cent (Baddeley et al., 1970). In addition, the long saphenous vein may be too narrow to achieve a satisfactory bypass or there may be no vein available because it is varicose or may have been removed in a stripping operation. We believe that EDFA is the first operation of choice for the treatment of most cases of femoropopliteal disease due to atherosclerosis.

The operation of extended deep femoral angioplasty

The details of the operation of EDFA have been described previously (Berguer et al., 1973). We have since introduced a major modification in *omitting the endarterectomy*. The operation we now perform is a simple incision of the common and deep femoral arteries to a point in the deep femoral artery where the vessel is reasonably free of disease, being soft and pliable. This may be as far down the artery as 15 cm from its origin. A vein or more often a Dacron patch is sewn into the deep femoral and common femoral arteries, the aim being to double the cross-sectional area of the deep femoral trunk. The main advantage of the omission of the endarterectomy is the avoidance of the possibility of intimal flap dissection at the distal end of the endarterectomy. Its omission greatly simplifies and shortens the operation. In our experience it has replaced the need for common to deep femoral artery autogenous vein bypass grafts (Berguer and Cotton, 1973).

Results

The results of 74 EDFA operations have been assessed in 72 patients (*Table I*) over the period from 1 April 1970 to 31 December 1973. A good result is shown by relief of claudication and rest pain and by the healing of gangrene either naturally or after minor amputation. Partial success means immediate relief of claudication and rest pain followed by the return of symptoms of ischaemia after an interval of some months. Failure of the operation was usually followed by a major amputation, though a few limbs were saved by femoropopliteal bypass. No patient operated on for claudication alone came to amputation.

---

* Department of Biomedical Engineering, King's College Hospital Medical School, London.

Good results (44 legs)
In this group (*Table II*) severe claudication (42 cases) and rest pain (34) were the commonest complaints. Gangrene of the toes (5) was less common. Ischaemic ulcers (6), sited at the malleoli, on the dorsum of the foot or on the heel, benefited from the operation. Two EDFA operations were successful after failed lumbar sympathectomy and 4 were successful after clotting of a femoropopliteal bypass graft.

Partial success (5 legs)
The operation was a success for a period of months after which rest pain returned. In 3 cases a lumbar sympathectomy was successful in relieving symptoms at intervals of 4, 5 and 6 months respectively after the primary operation. A remission of ischaemic symptoms has been prolonged in these cases over 9, 24 and 30 months respectively. In one case, following a failure of femoropopliteal bypass, a patch angioplasty was successful for only 1 month, following which a lumbar sympathectomy has relieved symptoms for a period of 30 months. In the last case the angioplasty was successful for a period of a year, when symptoms returned, necessitating a major amputation.

Failures (20 legs)
Twelve patients came to a major amputation. In one, failure was precipitated by rupture of the vein patch on the fourth postoperative day. Three legs were saved by femoropopliteal bypass. Five patients died; one from haemorrhage which was a direct result of the operation. The other deaths were due to cerebral haemorrhage, coronary thrombosis, bronchopneumonia and renal failure. The incidence of diabetes was 45 per cent in the failed cases and 14 per cent in the successful cases.

No change (5 patients)
This was the disappointing group. The patients were all claudicants and none would admit to any improvement in claudication distance. Their follow-up extended for a period of 12–40 months. All could have had a bypass operation but only one volunteered for a second operation—a vein bypass from the external iliac to the deep femoral artery which was successful. In this case it was not appreciated until after the EDFA operation that there was a degree of iliac artery stenosis. Once this was corrected the EFDA operation succeeded.

Duration of follow-up
The duration of follow-up in the successful cases is shown in *Table III*. The longest period of follow-up is 41 months. Thirty-three of the 44 limbs have remained satisfactory for periods from 10 to 39 months. Five-year patency rates have yet to be realized before the results of this operation can be compared with those of femoropopliteal bypass.

Table I: RESULTS OF EDFA

Result	No. of cases	%
Success	44	59·4
Partial success	5	7·5
Failure	20	25·6
No change	5	7·5

Table II: RESULTS RELATED TO CLINICAL PRESENTATION

Result	Total no.	Claudication	Rest pain	Gangrene	Ulcer	Diabetes
Success	44	42	34	5	6	6
Partial success	5	5	5	0	0	1
Failure	20	16	19	15	0	9
No change	5	5	0	0	0	1
Total	74	68	58	20	6	17

Table III: DURATION OF FOLLOW-UP OF SUCCESSFUL CASES

Follow-up (mth):	No. of cases:
0–9	8
10–19	15
20–29	8
30–39	12
40–49	1
Total	44

Table IV: CLAUDICATION DISTANCES AFTER EDFA

Claudication distance:	No. of cases:
Abolished	23
2 miles	1
1 mile	2
800 yd	4
400 yd	8
200 yd	3
<100 yd	3
Total	44

Table V: SUCCESS OR FAILURE OF EDFA RELATED TO AGE

Age (yr)	Failure	Success
40–49	1	2
50–59	5	17
60–69	8	16
70–79	5	9
80–89	1	0
Total	20	44

Table VI: ANGIOGRAPHY AS A GUIDE TO THE SUCCESS OF EDFA

	FPBP possible		FPBP not possible	
Result of EDFA	No.	%	No.	%
Success	34	60	6	10
Failure	5	9	12	21

FPBP, Femoropopliteal bypass.

Effect of EDFA on claudication
This proved better than had been expected. We had not thought it possible to improve claudication by merely

widening the trunk of the deep femoral artery, and yet, as can be seen in *Table IV*, there was a striking improvement in claudication distance. In the 44 successful cases claudication was completely relieved in 23 (52 per cent). In 92 per cent a claudication distance of more than 200 yards was achieved. In only 3 cases claudication distance was still limited to 100 yards.

Age and success

In *Table V* the association between age and success or failure is summarized. The numbers are small but it does not seem that there are significant differences between the two groups. Certainly it does not appear that younger patients fare less well than the aged.

Angiography and success and failure

Angiograms were available for analysis in 57 patients. They were interpreted without any knowledge of the result of the operation. The question to be answered from inspection of the radiographs was: Would a bypass have been possible or not? The results of inspection of the angiograms are summarized in *Table VI.* In 81 per cent of cases it was possible to predict success or failure of the operation of EDFA purely on the basis of a good or bad run-off. A good popliteal artery and a healthy trifurcation were almost always associated with a good result. Poor filling of the trifurcation and especially poor filling of the tibial arteries at the level of the midcalf were usually followed by failure. In 19 per cent of cases we could not predict the result. In 6 cases bypass was not possible and yet EDFA achieved a successful result. In 5 cases a bypass would have been possible but failure resulted. One of these cases was successfully treated by femoropopliteal bypass. The other cases could not have been treated by the bigger operation because their general condition was so poor.

Initially we requested oblique view angiograms of the deep femoral artery to reveal atherosclerotic lesions not seen on the anteroposterior view. We no longer take these oblique exposures because the artery is to be exposed and in general angiography tends to reveal less disease than that found at operation. In any event the purpose of the operation is to widen the deep femoral trunk without removing the atheromatous lesion.

Discussion

Until recently there have only been three operations for claudication, rest pain and gangrene due to atherosclerotic disease below the level of the inguinal ligament: femoropopliteal bypass, lumbar sympathectomy and amputation. Now EDFA adds a fourth possibility for which the indications have yet to be clearly defined. What does seem clear is that an EDFA operation can in many cases produce as good a result as a femoropopliteal bypass. From this series it seems that the clinical indications for EDFA are severe claudication, rest pain and ischaemic ulceration of the leg. Gangrene may be helped but less often than had been hoped.

Poor results of EDFA seem likely where there is a poor run-off in the angiograms, especially where the tibial arteries are not visualized. As would be expected, diabetics fare badly, as well as patients with extensive digital gangrene (*Table II*). The more severe the distal artery obstruction the less likely is a proximal arterial reconstruction to achieve success. Whether lumbar sympathectomy in combination with EDFA may offset this difficulty remains to be seen.

The advantages of EDFA are that it is simple and relatively free of complications. A striking advantage over femoropopliteal bypass is that swelling of the leg does not occur following EDFA, whereas although after bypass it may not be permanent it certainly lasts a year or so in the majority of cases.

All the patients surveyed in this paper had crippling claudication often associated with rest pain. The unexpected improvement in the former symptom raises the question as to whether the EDFA should be extended to patients who complain of a less severe claudication.

The haemodynamic effect of widening the trunk of the deep femoral artery to produce such a dramatic change in the arterial blood flow to the lower limb, and the value of flow and pressure measurement in these cases are the subjects of two further papers (Berguer et al., 1975; Roberts et al., 1975). Suffice it to say that the principle is to increase the surface area in the branching system of an arterial tree. What is needed for more precise definition of the indications for EDFA are methods of measuring the run-in and the run-off. It is hoped that modern non-invasive methods of measuring arterial circulation may be of value in determining the potential of arterial reconstruction. It is well known that claudication distance can increase spontaneously and in many cases the symptoms may disappear. Perhaps the operation of extended deep femoral angioplasty stimulates the processes of spontaneous resolution by augmenting flow into the collateral circulation.

Lastly, what are the indications for femoropopliteal bypass? We now believe it to be limited to cases of digital gangrene where the run-off permits a bypass to be done or where an EDFA has failed to produce improvement.

References

BADDELEY R. M., ASHTON F., SLANEY G. and BARNES A. D. (1970) Late results of autogenous vein bypass grafts in femoropopliteal arterial occlusion. *Br. Med. J.* **1**, 653–656.

BERGUER R. and COTTON L. T. (1973) Reversed autogenous saphenous vein bypass from the common to the deep femoral (profunda femoris) artery. *Br. J. Surg.* **60**, 676–679.

BERGUER R., COTTON L. T. and SABRI S. (1973) Extended deep femoral angioplasty. *Br. Med. J.* **1**, 469–471.

BERGUER R., HIGGINS R. F., ROBERTS V. C. and COTTON L. T. (1975) Haemodynamic analysis of extended deep femoral angioplasty. In the press.

COTTON L. T. (1971) Femoro-popliteal by-pass grafting—a fresh appraisal. Paper presented to the Annual Meeting of the Vascular Surgery Society of Great Britain, London.

MARTIN P., FRAWLEY J. E., BARABAS A. P. and ROSENGARTEN D. S. (1972) On the surgery of atherosclerosis of the profunda femoris artery. *Surgery* **71**, 182–189.

MARTIN P., RENWICK S. and STEPHENSON C. (1968) On the surgery of the profunda femoris artery. *Br. J. Surg.* **55**, 539–542.

ROBERTS V. C., QUICK C. R. G. and COTTON, L. T. (1975) Value of blood flow and pressure measurement in extended femoral angioplasty. In the press.

Br. J. Surg. Vol. 62 (1975) 344–347

Hydronephrosis complicating aortic reconstruction

GORDON HEARD AND GRAHAM HINDE*

SUMMARY

Prompted by an encounter with a symptomatic case, a study has been made of hydronephrosis complicating operations for aortic reconstruction.

Twenty patients operated upon consecutively for occlusive vascular disease and undergoing reconstructions involving the use of synthetic material in the vicinity of the ureter have been investigated by intravenous pyelography.

The incidence of hydronephrosis in pyelograms after a year or more was 10 per cent of the patients and 5·7 per cent of the ureters at risk. Dilatation, when it arose, was always apparent in the immediate postoperative period, but half of the dilatations evident at that time resolved within a year.

THERE have been few reports of hydronephrosis occurring in patients who have undergone abdominal arterial reconstruction. Lytton (1966) described 2 patients. In one a synthetic aorto-iliac bifurcation bypass had been complicated by the development of a left hydronephrosis, and in another there was bilateral ureteric obstruction which was more marked on the right. Thomford and Dorfman (1968) and Ehrlich et al. (1972) reported single cases in which the ureter lying between the prosthesis and iliac artery had become obstructed.

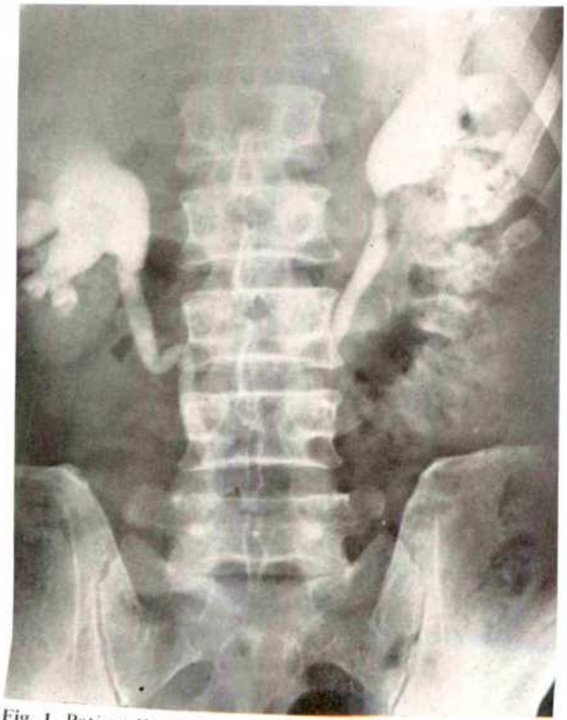


Fig. 1. Patient W. F. B. Intravenous pyelogram showing bilateral hydronephrosis.

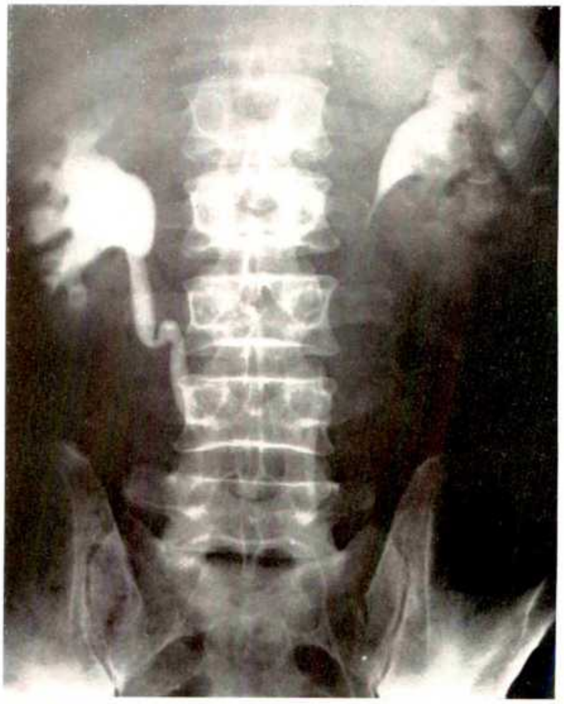


Fig. 2. Patient W. F. B. Intravenous pyelogram 1 month later showing resolution of the left hydronephrosis.

Case report

W. F. B., a male patient aged 49, presented with intermittent claudication due to bilateral aorto-iliac occlusion. Synthetic bypass of the lower aorta and common iliac arteries was carried out, with satisfactory restoration of pulses. The patient's postoperative course was uneventful but he returned at 2 months with frequency of micturition and loin pain. Intravenous pyelography showed bilateral hydronephrosi (*Fig.* 1). One month later the left renal tract had becom normal (*Fig.* 2). Further pyelograms showed slight improvemen on the right side, and at 18 months (*Fig.* 3) there was on slight residual fullness.

This being our first experience of the problem a finding no reported indication of its frequency clinical significance, the present study was embark upon.

A series of 20 patients undergoing aorto-iliac aortofemoral reconstruction involving the us synthetic tubes or patches in the vicinity of the u

---

* Departments of Surgery and Radiology, University H of Wales, Cardiff.

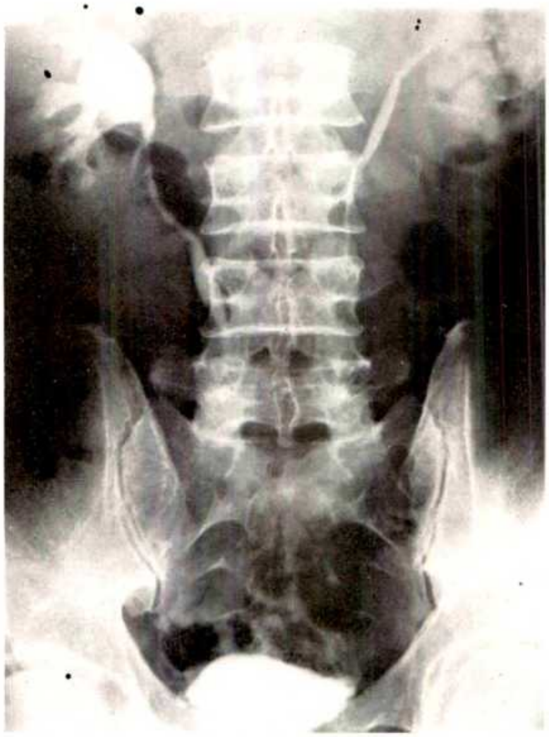


Fig. 3. Patient W. F. B. Intravenous pyelogram 18 months later showing improvement on the right side.

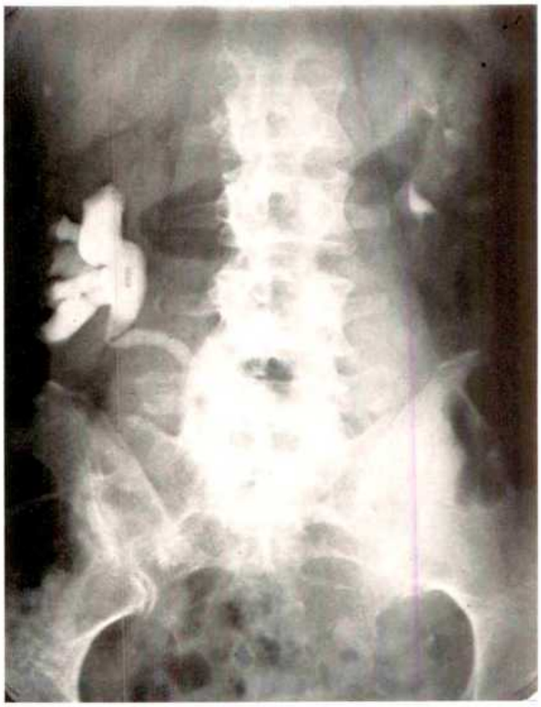


Fig. 4. Early postoperative intravenous pyelogram showing hydronephrosis on the right side.

and operated upon consecutively, has been investigated by intravenous pyelography. The indication in every case was occlusive arterial disease. No patient with aneurysm was included.

Findings

Preoperative pyelograms

These were carried out in 11 of the 20 patients. Only one was abnormal, displaying a slight fullness of the right renal pelvis of doubtful significance which remained unchanged in the late postoperative films.

Postoperative pyelograms

These were performed early (10–14 days) and late (after an interval of a year or more).

Early postoperative examinations were carried out in 13 of the 20 patients. There were 4 patients in whom hydronephrosis had developed, 3 on the right side (*Figs*. 4, 5, 6*a*) and 1 on the left (*Fig* 7*a*). Preoperative pyelograms had been undertaken and were normal in all 4 cases.

Late postoperative films were obtained in every patient. In 2 cases the earlier hydronephrosis had resolved (*Figs*. 6*b*, 7*b*), the other 2 persisting unchanged. In no patient did a hitherto undemonstrated hydronephrosis appear in the late pyelograms.

Type of operation performed

In 4 patients (with 7 ureters at risk) an aorta to external iliac synthetic bypass had been performed, and there were 2 instances of early hydronephrosis, 1 persisting (*Figs*. 4, 7).

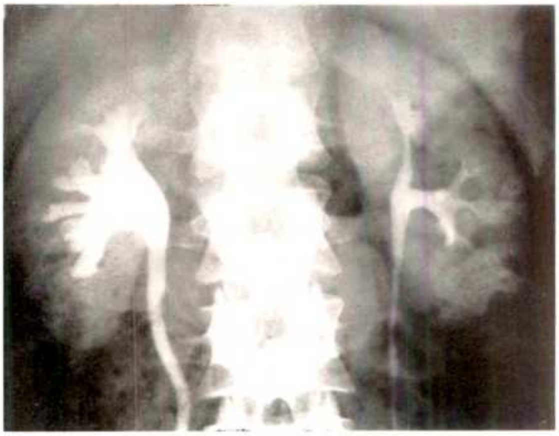


Fig. 5. Early postoperative intravenous pyelogram showing hydronephrosis on the right side.

In 12 patients (21 ureters at risk) an aortofemoral synthetic bypass had resulted in 1 early hydronephrosis persisting unchanged at 1 year (*Fig*. 5).

In 5 patients (7 ureters at risk) who had had a thrombo-endarterectomy and patching procedure of the aorta and common iliac artery, there was dilatation on the early pyelogram in 1 patient only and this resolved within the year (*Fig*. 6).

Relationship between ureter and reconstruction

Of 16 ureters left lying in front of the reconstruction, only 1 developed dilatation and this was transient. Of 13 ureters in which the position was not recorded, 2 showed a hydronephrosis, 1 being persistent at 1 year.

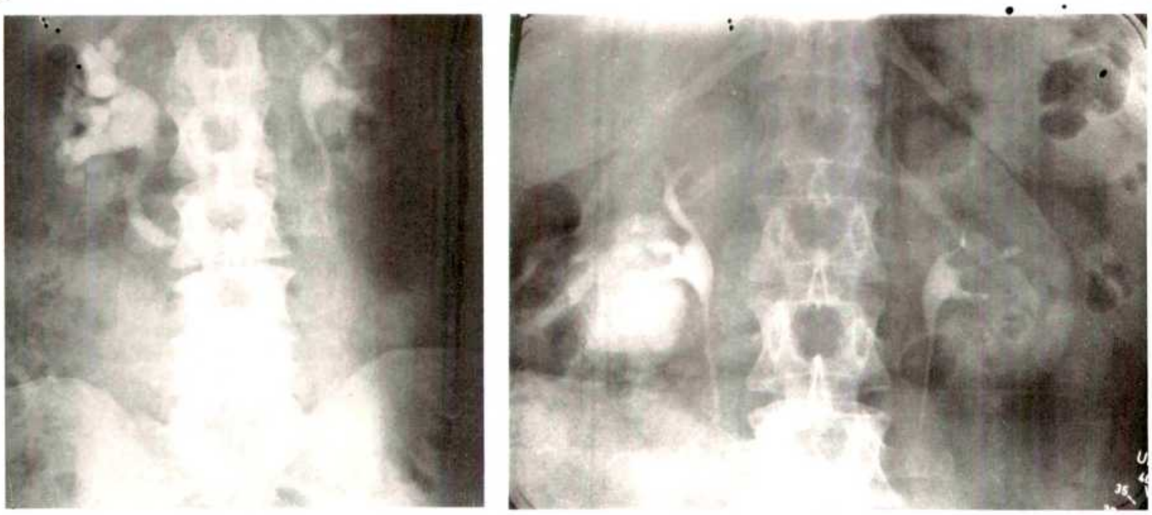


Fig. 6. *a*, Early postoperative intravenous pyelogram showing hydronephrosis on the right side. *b*, Late postoperative intravenous pyelogram showing resolution of the right hydronephrosis.

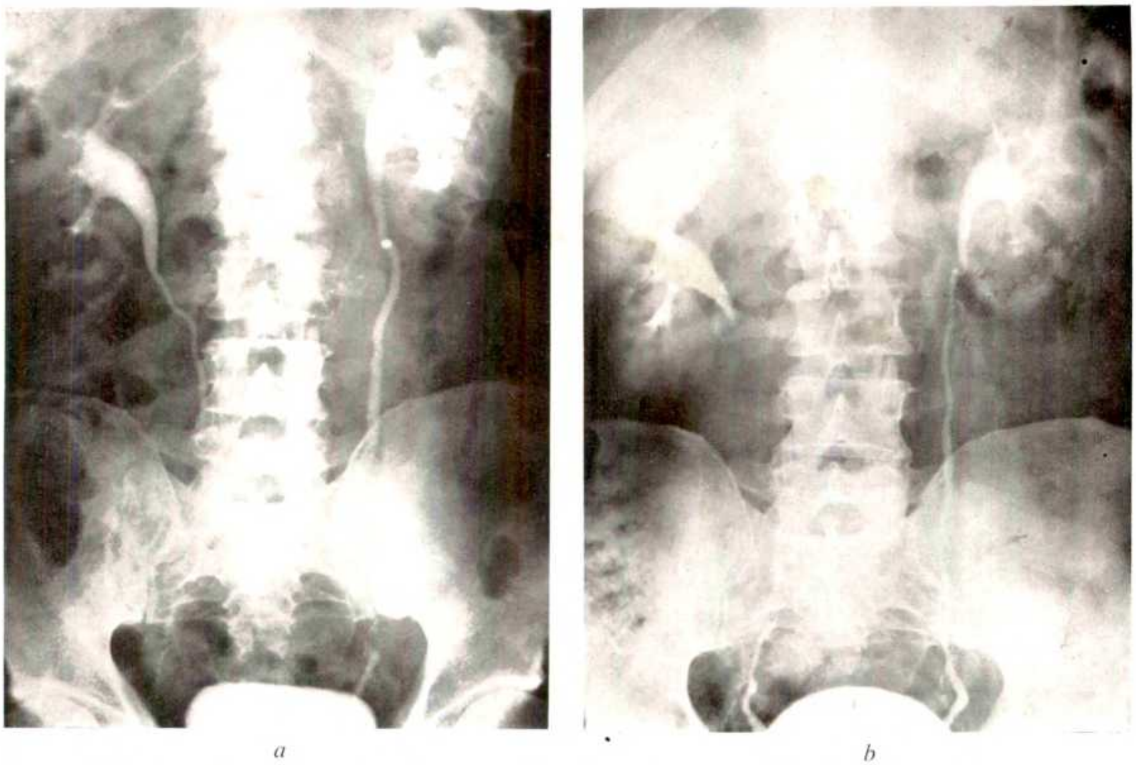


Fig. 7. *a*, Early postoperative intravenous pyelogram showing hydronephrosis on the left side. *b*, Late postoperative intravenous pyelogram showing resolution of the left hydronephrosis.

Of 6 ureters lying behind the prosthesis, 1 developed a hydronephrosis which was persistent in the late pyelogram.

Clinical features

None of the patients developing hydronephrosis had any symptoms which could be attributed to a urinary disorder.

Discussion

In 20 patients with 35 ureters at risk there was persistent dilatation in the late pyelograms in 2 patients, an incidence of 10 per cent of the patients or 5·7 per cent of the ureters at risk.

It would appear that if ureteric obstruction is going to arise it will do so in the early postoperative period. Neither patient with late hydronephrosis had a normal immediate postoperative pyelogram. This is also suggested by the findings in the patients reported by Lytton (1966) and by Thomford and Dorfman (1968) where pyelograms on the twelfth and sixteenth day showed the abnormality.

On the other hand, if obstruction is evident in the early postoperative films there is a good chance of later resolution. This was complete in 2 of the 4 instances. Complete resolution on one side and improvement on the other was also seen in the patient whose clinical presentation prompted this study.

The ureters may be involved in any form of reconstruction where foreign material is implanted, whether by a reconstruction behind the ureter or in a bypass behind or in front of the ureter. It is not possible from our observations to deny or confirm the suggestion made by Lytton (1966) and Thomford and Dorfman (1968) that the complication is more likely to arise if the ureter is left between the prosthesis and the iliac vessels.

It is presumed that the ureter becomes involved in the fibrous reaction around the prosthesis. Pulsatile compression may also play a part (Cockett et al., 1965).

There seems to be a higher risk where the distal vascular anastomosis is at iliac rather than femoral level (2 in 7 ureters at risk as against 1 in 21). This may be due to more extensive dissection of the ureter in such cases or to the ureter being caught in the angle between the graft and the vessel proximal to the anastomosis.

What measures may be taken to reduce the incidence of ureteric involvement in arterial reconstruction?

Although it cannot be regarded as of proved value, it would seem wise to place the ureter anterior to the graft when this can be done readily without excessive dissection and especially in the aorto-iliac bypass. When an aortofemoral procedure is being carried out blind digital dissection of the tunnels at the brim of the pelvis can leave the ureters either in front or behind, and more extensive exposure, particularly on the left side, may be necessary to be sure of the position of the ureter.

Fatty tissue, peritoneum or even omentum might be interposed between the ureter and the prosthesis, or the synthetic tube may be routed in such a way as to cross the ureter well above or below the pelvic brim. These alternatives deserve further study.

Detection of hydronephrosis following aortic reconstruction

All patients undergoing aorto-iliac and aortofemoral reconstruction should be subjected to pyelography in the early postoperative period. If the pyelogram is normal there is little likelihood of the later development of ureteric obstruction.

Management of established hydronephrosis

Where an early hydronephrosis is apparent a conservative attitude is justified, there being a 50 per cent chance of complete resolution within a year and a further chance of improvement.

In our 3 patients in whom hydronephrosis has persisted (i.e. 2 in the series and the case initially encountered) it has been mild in degree and not progressive. Active treatment has therefore not been indicated. The latter would, of course, be necessary in the event of progressive dilatation or impairment of renal function.

In Lytton's (1966) 2 cases and in the single cases of Thomford and Dorfman (1968) and Ehrlich et al. (1972) the ureter appeared to be compressed between the prosthesis in front and the iliac artery behind, and a ureterolysis with re-routing of the ureter anterior to the prosthesis was carried out in every case. However, while Lytton (1966) and Ehrlich et al. (1972) undertook and advocated re-routing by division and reanastomosis of the ureter, Thomford and Dorfman (1968) preferred to divide and reanastomose the prosthesis. The choice is not easy since, while division of the prosthesis carries the direct risk of vascular complications, division and anastomosis of the ureter might be followed by urinary leakage with some risk of infection of the adjacent synthetic prosthesis. There would also be the possibility of fibrous stricture at the site of the ureteric anastomosis.

References

COCKETT A. T. K., NAKAMURA R. M. and REIN B. I. (1965) The role of arterial pulsation in experimental hydronephrosis. *Invest. Urol.* **2**, 548–554.

EHRLICH R. M., HECHT H. L. and VEENEMA R. H. (1972) Chyluria following aorto-iliac bypass graft. *J. Urol.* **107**, 302–303.

LYTTON B. (1966) Ureteral obstruction following aortofemoral bypass grafts. *Surgery* **59**, 918–922.

THOMFORD N. R. and DORFMAN M. D. (1968) Ureteral obstruction caused by an aortofemoral bypass prosthesis. *Am. J. Surg.* **115**, 394–396.

Br. J. Surg. Vol. 62 (1975) 348–350

Small doses of subcutaneous sodium heparin in the prevention of deep vein thrombosis after elective hip operations*

VENOUS THROMBOSIS CLINICAL STUDY GROUP†

SUMMARY

The efficacy of small perioperative doses of subcutaneous heparin in preventing deep vein thrombosis has been studied in a controlled clinical trial on 64 patients undergoing elective hip surgery. The results indicate that the regimen of sodium heparin used was safe provided that the correct dose is given. It reduced the frequency of postoperative deep vein thrombosis from 37 to 7 per cent.

THE incidence of deep vein thrombosis after operations on the hip is high (Field et al., 1972; Kakkar et al., 1972). Because it is known that quantities of heparin insufficient to alter the overt ability of the blood to clot (5000 units 12-hourly) reduce the incidence of deep vein thrombosis in general surgical, thoracic and gynaecological patients (Williams, 1971; Gordon-Smith et al., 1972; Kakkar et al., 1972; Nicolaides et al., 1972; Ballard et al., 1973; Gallus et al., 1973), this technique has also been applied to those having either emergency or elective hip operations, but apparently without effect (Kakkar et al., 1972). A slightly more frequent dose of heparin (5000 units 8-hourly) has been shown to halve the incidence of thrombosis (detected by the ^{125}I-fibrinogen test) in patients operated upon for fracture of the femoral neck (Gallus et al., 1973), but subsequent trials produced conflicting results (Hampson et al., 1974; Morris et al., 1974). This paper reports a study of an 8-hourly regimen in patients undergoing elective operations on the hip.

Patients and methods

Sixty-four patients who were to undergo elective hip operations (total hip replacement) were admitted to the trial and were allotted to either a control or treatment group by drawing envelopes. All received the hospital routine of supervised leg and breathing exercises before and after operation and were made to walk with crutches on the first postoperative day. In the treatment group sodium heparin (5000 units in 0·2 ml) was given subcutaneously 2 hours before operation and thereafter 8-hourly for 10 days by the method previously described (Griffith and Boggs, 1964; Nicolaides et al., 1972). The amount of blood transfused at operation and the quantity of the suction drainage from the wound in the first 24 hours were measured.

The diagnosis of deep vein thrombosis in the calf of the affected limb and distal to the inguinal ligament on the opposite side was made by the ^{125}I-fibrinogen test using a Pitman 235 isotope localization monitor (Kakkar et al., 1970). Patients were considered to have deep vein thrombosis when an increase of 20 was observed in the percentage value of radioactivity (in the calf of the operated limb and in the calf or thigh of the opposite limb) at the same place on two different days or between two adjacent sites, provided that this increase persisted for more than 24 hours. Patency of the deep veins between the popliteal and inferior vena cava was tested on the fifth and tenth days after operation with an ultrasound generator using the Doppler principle (Parks blood flow detector, Model 801). Changes in the blood velocity during quiet breathing, during a Valsalva manœuvre and on compressing the calf and thigh muscles were recorded. The veins were considered to be patent when the flow in the femoral vein in the groin was phasic with respiration, stopped at the height of Valsalva and increased in velocity with muscle compression while the long saphenous vein was occluded at the knee. Venography was done when the ^{125}I-fibrinogen test indicated deep vein thrombosis in the popliteal or more proximal veins, or on evidence of venous occlusion from ultrasound examination.

Table I: INCIDENCE OF DEEP VEIN THROMBOSIS

	No. of patients		
Group	Admitted	Excluded	DVT
Control	30	0	11
Test	34	4*	2

DVT, Deep vein thrombosis. Fisher's exact test, $P = 0{\cdot}0046$.

* A heparin injection was accidentally omitted in 3 patients and severe bleeding from heparin overdose occurred in 1 patient.

Results

Sixty-four patients were admitted to the trial; 4 were subsequently excluded for the following reasons. In 3 patients a dose of heparin was omitted. One patient had a severe haemorrhage on the third postoperative day as a result of a large dose of heparin given in error. Heparin was discontinued and the patient was excluded from the trial. None of these patients

---

* Based on a paper presented to the Surgical Research Society of Great Britain and Ireland in January 1974.

† Members: A. N. Nicolaides, P. A. Dupont, D. C. S. Parsons, J. D. Lewis, S. Desai, M. Appleberg, F. T. Horan, C. J. Walker, M. K. D. Benson, D. C. Jameson Evans, J. Miller, K. M. Esah.

Surgical Unit and Department of Orthopaedic Surgery, St Mary's Hospital, London.

Table II: DISTRIBUTION OF FACTORS PREDISPOSING TO DEEP VEIN THROMBOSIS AND THEIR RELATIVE RISKS

	Risk factors and their weights*				
	Carcinoma (0·19)	Obesity (0·38)	Previous DVT (0·69)	Varicose veins (0·60)	Sum of (weight × number of patients) of all risk factors
Number of patients in control group	0	10	4	4	8·96
Number of patients in test group	1	12	2	4	8·53
Difference between the two groups	−1	−2	+2	0	0·43†

DVT, Deep vein thrombosis.

* Weights are expressed as the natural logarithm of relative risk.

† The relative risk in the unmatched patients of the control group is given by the antilogarithm of 0·43 = 1·5, i.e. the increased risk in the control group is approximately equivalent to 1 patient.

Table III: AMOUNT OF BLOOD TRANSFUSED, POSTOPERATIVE BLOOD LOSS AND INCIDENCE OF WOUND HAEMATOMA

Group	Blood transfused* (mean no. of units ± s.d.)	Suction drainage* (mean no. of ml ± s.d.)	Wound haematoma (no. of patients)
Control	2·0 ± 0·69	333 ± 233	3
Test	2·4 ± 0·64	388 ± 104	4

* *t* test, $P > 0{\cdot}05$.

developed thrombosis as detected by the ^{125}I-fibrinogen test. Of the remaining 60 patients, 30 were in the control group and 30 in the heparin group. The frequency of deep vein thrombosis was 11 out of 30 (37 per cent) in the control group and 2 out of 30 (7 per cent) in the test group (*Table I*). This difference was highly significant (Fisher's exact test, $P = 0{\cdot}0046$). In the 2 patients in the test group who developed thrombosis the thrombus occurred in the operated leg and remained confined to the calf. In the control group all the thrombi were first detected in the calf. Thrombosis was bilateral in 4 patients, occurred in the operated leg only in 4 patients and in the opposite leg only in 3 patients. There were thus 15 limbs with thrombosis. In 3 (20 per cent) of these the thrombotic process extended proximally. This extension was into the popliteal vein in one, into the superficial femoral in one and into the iliofemoral segment in another patient. The last was detected with Doppler ultrasound. In these 3 patients the diagnosis was confirmed by venography and the patient was immediately confined to bed and treated with a continuous intravenous infusion of heparin (10 000 units 6-hourly for 48 hours) and oral anticoagulants. None of these or any other patients in this trial developed clinical evidence of pulmonary embolism.

The control and test groups were comparable for age (mean age and standard deviation: control group 64 ± 11·9; test group 63 ± 12·3), but not for weighted risk factors (cancer, obesity, previous deep vein thrombosis, varicose veins), as shown in *Table II*. The use of weights for risk factors calculated from previous data (Nicolaides et al., 1973) is subject to criticism that a different population may be under study, but they express relative risk and as such are independent of the incidence of thrombosis. If a correction is made for the increased risk in the control group the results will still be significant (Fisher's exact test: $P = 0{\cdot}0094$). The amount of blood transfused, postoperative blood loss and incidence of wound haematoma in the two groups were comparable (*Table III*).

Discussion

Low dose heparin probably works by enhancing the activity of antithrombin III (Damus et al., 1973; Wessler and Yin, 1973) in forming complexes with serine proteases such as activated factors X and XI, thus rendering them incapable of taking part in the coagulation cascade. If heparin is administered before these factors are activated by events which accompany local tissue trauma and the general effects of injury, then only small quantities are needed to prevent intravascular thrombosis and, as this study suggests, to reduce its tendency to extend. The plasma level of heparin produced by 5000 units given subcutaneously 2 hours before operation becomes too low to be detected within about 6 hours (Kakkar et al., 1972), even when the most sensitive method is used (Wessler et al., 1971). However, the blood transfusion requirements are increased in patients undergoing abdominal and thoracic operations when this dose of heparin is administered 8-hourly (Gallus et al., 1973), which suggests that clotting is less efficacious than normal. Thus, though it is theoretically desirable to administer heparin 5–6-hourly, a reasonable compromise between prophylaxis of deep vein thrombosis and the risk of bleeding is an 8-hourly regimen. Our evidence suggests that the increased tissue trauma and the increased immobility imposed on the patient undergoing hip operations necessitate such a regimen, in contrast to the patients subjected to operations on soft tissues (Williams, 1971; Gordon-Smith et al., 1972; Kakkar et al., 1972; Nicolaides et al., 1972; Ballard et al., 1973; Gallus et al., 1973).

We do not have evidence that morbidity is increased by the use of low dose heparin, but there is in this therapy the ever-present risk of overdose which did occur in one of our patients. If this preventive measure is to be widely adopted, a method such as the use of disposable cartridges containing the correct dose should be sought to eliminate human error. Further, it is a commentary on human frailty that in 3 patients the heparin was omitted even though we were carrying out a trial where supervision might have been expected to be adequate. It may well be that the universal or near universal use of heparin in this manner (or for that matter any other form of blanket prophylaxis such as preventive antibiosis for wound infection) will fail to achieve the theoretically maximum effect because it cannot be made free of human error. Concentration on the evaluation of risk and the selective use of prophylaxis in patients seriously in danger may ultimately prove a more attractive strategy. Certainly we would not wish our results to be construed at this stage as an argument for the widespread use of heparin in the prophylaxis of deep vein thrombosis in hip surgery.

This caveat is the more true in that two questions remain unanswered. First, does the use of low dose heparin affect the incidence of pulmonary embolism? The reduction in the incidence of thrombosis in the axial veins of the leg shown in this and other studies (Williams, 1971; Gordon-Smith et al., 1972; Kakkar et al., 1972; Nicolaides et al., 1972; Ballard et al., 1973; Gallus et al., 1973), and the results of earlier work on the incidence of pulmonary embolism by Sharnoff (Sharnoff and De Blasio, 1970) suggest that this should be so, but a larger investigation will be required to provide statistical confirmation. Secondly, what is the incidence and clinical pattern of deep vein thrombosis later in convalescence after hip surgery, for example in the second or third week? A venographic study suggests that half of all patients may have thrombi in leg veins at this time and that many of the thrombi are in the femoral and more proximal veins (Johnson, 1974). In a recent clinical trial a large number of thrombi developed in the second postoperative week after heparin therapy was discontinued (Hampson et al., 1974). Further trials are needed to test the wisdom of prophylaxis throughout the patient's stay in hospital.

Acknowledgements

We would like to express our grateful thanks to the consultant orthopaedic surgeons at St Mary's Hospital for allowing us to study their patients; Miss Lynne Pentlow, Miss Daphne Faulkner and Miss Elaine Billing for their technical assistance; the Board of Governors of St Mary's Hospital, Pfizer Ltd (UK) and Weddel Pharmaceuticals Ltd for financial support.

References

BALLARD R. M., BRADLEY-WATSON P. J., JOHNSTON F. D., KENNEY A., MCCARTHY T. G., CAMPBELL S. and WESTON J. (1973) Low doses of subcutaneous heparin in the prevention of deep vein thrombosis after gynaecological surgery. *J. Obstet. Gynaecol. Br. Commonw.* **80**, 469–472.

DAMUS P. S., HICKS M. and ROSENBERG R. D. (1973) Anticoagulant action of heparin. *Nature (Lond.)* **246**, 355–359.

FIELD E. S., NICOLAIDES A. N., KAKKAR V. V. and CRELLIN R. Q. (1972) Deep-vein thrombosis in patients with fractures of the femoral neck. *Br. J. Surg.* **59**, 377–379.

GALLUS A. S., HIRSCH J., TUTTLE R. J., TREBILOCK R., O'BRIEN S. E., CARROLL J. J., MINDEN J. H. and HUDECKI S. M. (1973) Small subcutaneous doses of heparin in prevention of venous thrombosis. *New Engl. J. Med.* **288**, 545–551.

GORDON-SMITH I. C., GRUNDY D. J., LE QUESNE L. P., NEWCOMBE J. F. and BRAMBLE F. J. (1972) Controlled trial of two regimens of subcutaneous heparin in prevention of postoperative deep vein thrombosis. *Lancet* **1**, 1133–1135.

GRIFFITH G. C. and BOGGS R. B. (1964) The clinical usage of heparin. *Am. J. Cardiol.* **14**, 39–46.

HAMPSON W. G. J., HARRIS F. C., KEITH LUCAS H., ROBERTS P. H., MCCALL I. W., JACKSON P. C., POWELL N. L. and STADDON G. E. (1974) Failure of low-dose heparin to prevent deep-vein thrombosis after hip-replacement arthroplasty. *Lancet* **2**, 795–797.

JOHNSON R. (1974) Personal communication.

KAKKAR V. V., CORRIGAN T., SPINDLER J., FOSSARD D. P., FLUTE P. T., CRELLIN R. Q., WESSLER S. and YIN E. T. (1972) Efficacy of low doses of heparin in prevention of deep-vein thrombosis after major surgery. *Lancet* **2**, 101–106.

KAKKAR V. V., NICOLAIDES A. N., RENNEY J. T. G., FRIEND J. R. and CLARKE M. B. (1970) ^{125}I-labelled fibrinogen test adapted for routine screening for deep-vein thrombosis. *Lancet* **1**, 540–542.

MORRIS G. K., HENRY A. P. J. and PRESTON B. J. (1974) Prevention of deep-vein thrombosis by low-dose heparin in patients undergoing total hip replacement. *Lancet* **2**, 797–799.

NICOLAIDES A. N., DUPONT P. A., DESAI S., LEWIS J. D., DOUGLAS H. N., DODSWORTH H., FOURIDES G., LUCK R. J. and JAMIESON C. W. (1972) Small doses of subcutaneous sodium heparin in preventing deep venous thrombosis in major surgery. *Lancet* **2**, 890–893.

NICOLAIDES A. N., IRVING D., PRETZELL M., DUPONT P., LEWIS J., DESAI, S., DOUGLAS J. N., KAKKAR V. V. and FIELD E. S. (1973) The risk of deep-vein thrombosis in surgical patients. *Br. J. Surg.* **60**, 312.

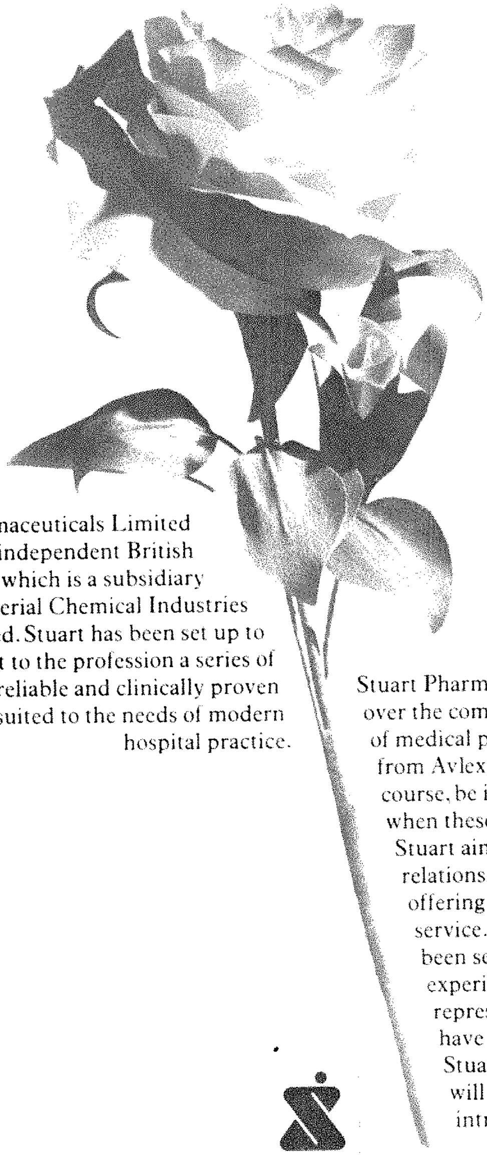
SHARNOFF J. G. and DE BLASIO G. (1970) Results in the prophylaxis of postoperative thromboembolism. *Lancet* **2**, 1006–1007.

WESSLER S. and YIN E. T. (1973) Theory and practice of minidose heparin in surgical patients. *Circulation* **47**, 671–676.

WESSLER S., YIN E. T. and BUTLER J. W. (1971) A new sensitive method of heparin assay. *Circulation* **44**, Suppl. 11, 79 (Abstr.).

WILLIAMS H. T. (1971) Prevention of postoperative deep-vein thrombosis with perioperative subcutaneous heparin. *Lancet* **2**, 950–952.

Stuart
blossoms

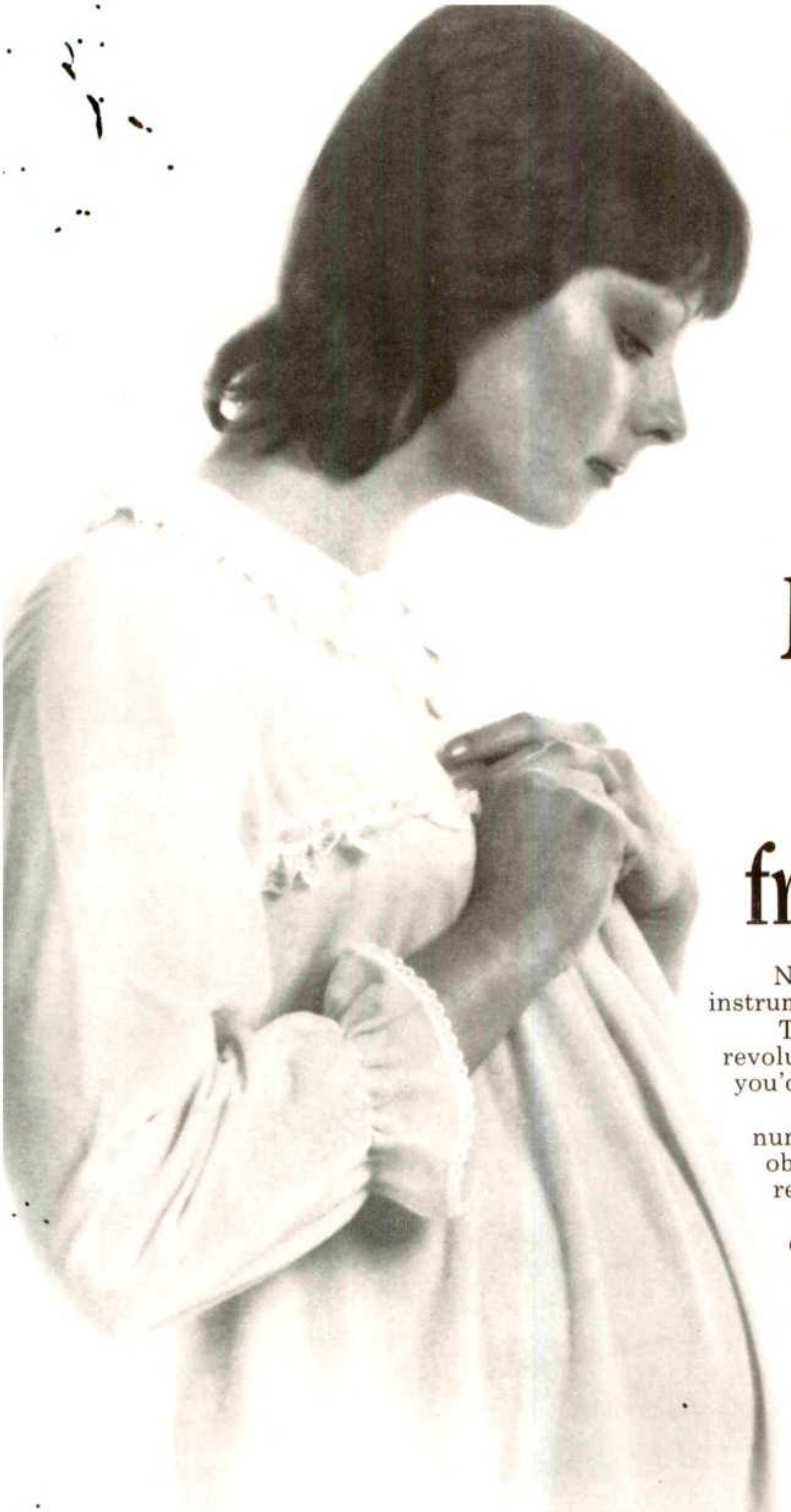


Stuart Pharmaceuticals Limited is a new, independent British Company which is a subsidiary Company of Imperial Chemical Industries Limited. Stuart has been set up to present to the profession a series of reliable and clinically proven products suited to the needs of modern hospital practice.

Stuart Pharmaceuticals will, over the coming year, market a variety of medical products currently available from Avlex Limited. You will, of course, be informed separately as and when these changes occur.

Stuart aims to develop a good working relationship with the profession by offering an efficient and courteous service. To ensure this all staff have been selected for their previous experience and before any Stuart representative calls on you he will have received extensive training in the Stuart range of products. Now if you will kindly turn over the page we will introduce the first of our products.

STUART



For Mother's Day...

from Seward.

Now there is a Seward range of instruments for gynaecology and obstetrics.

There's nothing particularly revolutionary about it. Yet it's everything you'd expect from Seward.

We worked closely with quite a number of leading gynaecologists and obstetricians and analysed their requirements down to the last detail.

That's why the new range is exceptionally comprehensive. Around 400 instruments altogether. All made in England—to the same exacting quality standards as all ou other instruments.

We carry ample stocks of our new gynaecology and obstetrics range. So we can supply whatever you need remarkably fast—normally within just a few days.

Now it could mean one less problem delivery for you to worry about.

seward–the fast word in quality

A. J. Seward, UAC House, Blackfriars Road, London SE1 9UG.
Telephone: 01-928 7444
A member of the Medical Division of UAC International

DISPRAY I
Trade Mark
Quick Prep
Chlorhexidine gluconate 0.5% w/v in 70% I.M.S.
Stuart Pharmaceuticals Limited Cheadle, Cheshire.
DISPRAY 2
Trade Mark
Hard Surface Disinfectant
Chlorhexidine gluconate 0.02% w/v in 70% I.M.S.
Stuart Pharmaceuticals Ltd Cheadle, Cheshire.

DISPRAY I

TRADE MARK

Quick Prep

Chlorhexidine Gluconate 0.5% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for skin disinfection

'Dispray' 1 Quick Prep. (formerly known as Hibispray 1) is an ideal preparation for skin and hand disinfection in the busy hospital environment.

At the touch of a button it gives fast, easy and economical skin disinfection prior to surgery, injection or venepuncture.

When colour delineation is required eg. pre-operatively, 'Dispray' 3 is available with a red dye.

The 'Dispray' range combines effectiveness with convenience and economy.

Instant Availability.
No solutions to prepare.

Easy to use.
No swabs or bottles required.

Quick and Effective.
Rapid bactericidal action.

Efficient Application.
No wasted solutions.

Contents cannot be contaminated.
No rejected solutions.

Long Lasting.
Contents of one can treat 100sq. ft.

'Dispray' 1, 2, 3.
The Pick of the Bunch for Disinfection.

DISPRAY 2

TRADE MARK

Hard Surface Disinfectant

Chlorhexidine Gluconate 0.02% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for hard surface disinfection

'Dispray' 2 Hard Surface Disinfectant (formerly known as Hibispray 2) provides rapid disinfection of all hard surfaces throughout the hospital. Trolleys, cabinets, cupboards, working surfaces – even footwear, are rapidly, effectively and efficiently disinfected.

Further information is available from:

STUART

Stuart
Pharmaceuticals
Limited.
Carr House,
Carrs Road,
Cheadle,
Cheshire SK8 2EG.

Your hands are your most important instruments-
it pays to take care of them

The obvious fact that a surgeon's hands are of prime importance to his work was borne in mind when 'Hibiscrub' was formulated. 'Hibiscrub' is designed to keep hands healthy, even after repeated use.

However, the prime importance of a handwash is effectiveness: rapid prolonged bactericidal action against skin bacteria is assured by the presence of the well-proven antiseptic 'Hibitane'.

"These studies have shown that a 4% chlorhexidine detergent solution ['Hibiscrub'] is a potentially outstanding addition to the small list of detergent-disinfectant preparations for the hands of surgeons and nurses, with a greater immediate effect than that obtained with the hexachlorophane or even the iodophor preparations."
British Medical Journal, (1973), 1, 510.

hibiscrub

RAPID BACTERICIDAL SKIN CLEANSER

Contains 'Hibitane' Chlorhexidine Gluconate 4% w/v.

ICI Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

'Hibitane' and 'Hibiscrub' are trade marks.

PH828

Br. J. Surg. Vol. 62 (1975) 351–353

The construction of a skin-lined hemithorax in pigs

LADE WOSORNU*

SUMMARY

The feasibility of creating a skin-lined hemithorax was tested in 6 pigs. All the pigs survived intrapleural skin grafting, and within 3 weeks they doubled their mean initial weight from 16·0 ± 1·6 kg to 32·4 ± 2·6 kg. In 4 (out of 4) pigs the skin-lined cavity was opened successfully to the exterior; it had reproduced closely the contour of the hemithorax. It is concluded that it is feasible to construct a skin-lined hemithorax with a mean volume of 276·0 ± 19·6 ml in pigs, whose mean body weight was 37·5 ± 2·5 kg. This confirms earlier work in the rat.

It has been shown in short-lived experiments that it is feasible to implant prosthetic lungs (Bodell et al., 1965). Peirce (1966) suggested that if the pleural cavity were to house prosthetic organs permanently, it must first be exteriorized by lining it with silicone 'skin'. After showing that autogenous skin was more suitable as the new pleural lining, Wosornu (1972) described a reproducible technique for transforming the left hemithorax of Specific Pathogen Free rats into stable skin-lined cavities.

When it was found that the cavities could be opened to the exterior without embarrassing breathing in the contralateral lung, the experimental preparation was put forward as a model of a cavity which could be employed to house prosthetic organs inside the thorax.

The aim of the present experiments was to see whether it was feasible to use this technique to create similar cavities in a larger animal. A series of experiments identical in design to those described in the rat (Wosornu, 1972) were carried out on 6 pigs.

Materials and methods

Six pigs (4 male and 2 female) were employed. They were mixed Landrace strain of mean initial weight 16·0 ± 1·6 kg. They were kept under standard laboratory conditions in sties fitted with infrared lamps so that temperatures of 30 °C could be reached—an important consideration in the immediate postoperative period. They were fed once a day with 2 kg of concentrated pig food (Spillers, London), and the drinking water was replenished as required.

Under general anaesthesia autogenous skin bags were grafted into the pleural space. Anaesthesia was induced by halothane/air mixture using the technique described by Singh et al. (1971). The pigs were intubated and anaesthesia was maintained by positive pressure ventilation with the Palmer Ideal respirator.

Operative procedure

The shoulders and gluteal regions were prepared surgically for use as donor sites and split skin grafts were taken with a Humby knife. With 2/0 atraumatic silk, the sheets of skin were sutured together to form skin bags such that the hair-bearing surfaces were enclosed completely. A silicone tube 40 cm long (outer diameter 3 mm) was employed as an internal splint to give a roughly rectangular shape to the skin bag. The initial weight of the pigs and the size of the skin bags are given in *Table I.*

In the lateral position the left chest was opened through the bed of the unrestricted 5th rib. Bleeding was slight. The skin bag was laid inside the pleural space making sure that it reached the apex. The lungs were expanded and the chest was closed in layers without drainage. During the closure the lungs were inflated repeatedly. At the end of the operation 5 mega-units of crystalline penicillin were given by intramuscular injection, the chest wound and donor sites were sprayed with Nobecutane and the pig was returned to the warm sty. Intramuscular crystalline penicillin was repeated for the next 5 days (dose: 1 mega-unit once a day). Requiring hardly any supervision, the pigs resumed normal feeding the day after the operation.

Table I: WEIGHT OF PIGS AND SIZE OF SKIN BAGS

Pig no.	Initial body weight (kg)	Size of skin bag (mm)
1	21·3	125 × 125
2	18·2	163 × 75
3	18·2	180 × 85
4	12·7	138 × 113
5	10·9	138 × 76
6	14·3	125 × 75

Observations on the pigs with the skin-lined hemithorax closed

The pigs' general progress was observed and they were weighed once a week for 3 weeks; the skin-lined hemithorax was demonstrated radiologically; and the pressure inside the cavity was measured and compared with the normal pleural pressure.

Under radiographic control 20 ml of 45 per cent hypaque were injected into the skin-lined hemithorax on the tenth postoperative day in the first 3 pigs and chest X-ray films were taken. The procedure was repeated at the end of the third week in all 6 pigs. One of these pigs was then sacrificed for histological examination. On each occasion light general anaesthesia without intubation was employed. The pressure in the pleural cavities was measured in 5 pigs with a strain gauge manometer.

---

* Royal Postgraduate Medical School, Hammersmith Hospital, London.
Present address: University of Ghana Medical School, P.O. Box 4236, Accra, Ghana.

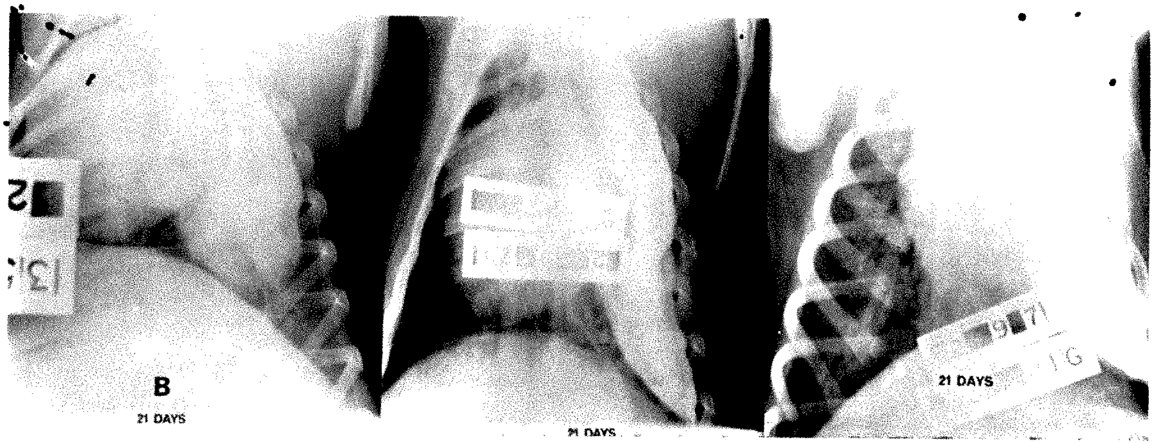


Fig. 1. Anteroposterior chest X-ray films taken in the third postoperative week (pig nos 1–3). The skin-lined hemithorax was outlined with 20 ml of 45 per cent hypaque. Fluid had accumulated in and had remained confined to the closed skin-lined cavity, the lung bases being clear on the X-ray films. The cavities had become nearly co-extensive with the hemithorax. The shape, however, varied from pig to pig. Mediastinal shift was moderate and the right lung fields were normal.

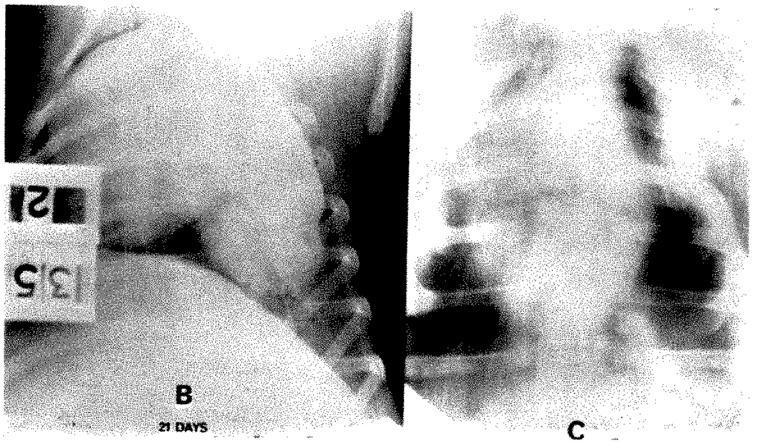


Fig. 2. Anteroposterior chest X-ray films of pig no. 3 before and after opening the skin-lined hemithorax to the exterior. *B*, The closed skin-lined hemithorax was outlined with 20 ml of hypaque at 3 weeks. *C*, Two weeks later the cavity was opened to the exterior. The intrapleural skin graft had closely reproduced the contours of the left hemithorax and the right lung field remained normal on both X-ray films.

Opening the skin-lined hemithorax to the exterior

The skin-lined hemithorax was opened to the exterior 5 weeks after intrapleural skin grafting. The pigs were anaesthetized and intubated as a precaution against protracted breath-holding. Pig no. 4 failed to survive intubation, which is sometimes a difficult technique because of the peculiar anatomy of the pig's larynx.

Anaesthesia was induced with halothane/air mixture and supplemented with intravenous pentobarbitone sodium (10 mg/kg). A disc of skin about 4 cm in diameter was excised from the 4th left intercostal space about 10 cm from the sternum. The intercostal muscles were excised to expose the thick, pearly white, skin-reinforced parietal pleura, a disc of which was excised; it measured about 15 mm in diameter. After the fluid in the skin-lined hemithorax was aspirated and its volume measured, chest X-ray films were taken.

Before and after opening the skin-lined hemithorax to the exterior, the following variables were measured: systemic blood pressure; electrocardiogram; arterial pH, $P\text{O}_2$ and $P\text{CO}_2$; and tidal air from the trachea and the skin-lined hemithorax. Details of these measurements will be described elsewhere.

Results

All 6 pigs survived the operation of intrapleural skin grafting. Their postoperative recovery was swift and uneventful. In the first 3 postoperative weeks the pigs doubled their mean initial weight from 16·0 ± 1·6 kg to 32·4 ± 2·6 kg. In 4 (out of 4) pigs the skin-lined hemithorax was successfully opened to the exterior. X-ray films of the skin lined hemithorax before and after thoracostomy are shown in *Figs.* 1 and 2. Paired data on pleural pressure were available for 5 pigs (*Table II*). *Table III* shows the volume of the skin-lined hemithorax 5 weeks after intrapleural skin grafting.

Table II: PLEURA PRESSURE IN (A) NORMAL PLEURA AND (B) CLOSED SKIN-LINED HEMITHORAX

	Pleural pressure (cm H_2O)					
	End of expiration		End of inspiration		Mean pressure	
Pig no.	A	B	A	B	A	B
2	5·0	8·0	−12·0	−10·0	−4·0	1·0
3	1·0	7·0	−15·0	− 7·0	−4·5	1·0
4	2·0	8·0	−10·5	− 8·0	−4·0	0·5
5	3·0	6·0	−10·0	− 4·0	−5·5	2·0
6	−2·0	4·0	−10·0	− 4·0	−6·0	2·0
Mean	1·8	6·6	−11·5	− 6·6	−4·8	1·3
s.e.m.	1·16	0·75	0·94	1·17	0·4	0·3
t	6·53		4·28		8·76	
P (d.f. = 4)	0·003*		0·013*		0·0009*	

* Significant.

Table III: WEIGHT OF PIGS AND VOLUME OF SKIN-LINED HEMITHORAX 5 WEEKS AFTER INTRAPLEURAL SKIN GRAFTING

Pig no.	Weight (kg)	Volume (ml)
2	36·8	255
3	41·4	230
4	40·1	340
5	28·2	255
6	40·9	300
Mean	37·48	276
s.e.m.	2·45	19·58

The implanted skin capsules 'took' on the surrounding intrathoracic structures, reproducing closely the outline of the hemithorax (*Fig.* 2). The average mean pressure in the closed skin-lined hemithorax was 1·3 ± 0·3 cm H_2O, compared with the average mean pressure of −4·8 ± 0·4 cm H_2O in the normal hemithorax ($P < 0·001$).

In 5 pigs of mean body weight 37·5 ± 2·5 kg, the mean volume of the skin-lined hemithorax was 276·0 ± 19·6 ml. This compared with a mean volume of 7·4 ± 0·3 ml in 15 rats of mean body weight 298·3 ± 9·0 g in an earlier series (Wosornu, 1971).

Conclusion

It was concluded that a technique which allowed the construction of a skin-lined hemithorax in rats is appropriate to a larger animal, the pig. Cavities with a volume of approximately 300 ml could be achieved in pigs with a mean weight of 37·5 kg. Such cavities compare with those in rats of mean weight of 298·3 g when average volumes of 7·4 ml were achieved.

Acknowledgements

I am grateful to Professor D. G. Melrose and Professor R. B. Welbourn for advice and encouragement, and to Mrs J. Becket and Messrs E. Williams, R. Elliott and D. Wilson for technical assistance.

References

BODELL B. R., HEAD J. M., HEAD L. R. and FORMOLO A. J. (1965) An implantable artificial lung. *JAMA* **191**, 301–303.

PEIRCE E. C. II (1966) *Trans. Am. Soc. Artif. Intern. Organs* **12**, 334.

SINGH M. P., ELLIOTT R. L. and MELROSE D. G. (1971) A simple technique of anaesthesia for experimental open-heart surgery in the calf. *Thorax* **26**, 103–107.

WOSORNU L. (1971) MD Thesis, University of Glasgow.

WOSORNU L. (1972) A technique for creating a skin-lined hemithorax. *Br. J. Surg.* **59**, 868–872.

Br. J. Surg. Vol. 62 (1975) 354–355

Postvagotomy dysphagia

J. D. SPENCER*

SUMMARY

Following truncal vagotomy some patients develop dysphagia, which rarely can progress to complete obstruction. It has been postulated that haematoma formation in the tissues surrounding the lower oesophagus may lead to peri-oesophageal fibrosis and compression of the lumen of the oesophagus. This has been confirmed by open operation in only a few patients. A case is described in which oesophageal obstruction occurred 3 weeks after a vagotomy and pyloroplasty had been performed.

Case report

The patient was a 39-year-old West Indian male whose 8-year history of peptic ulcer symptoms had not been fully controlled by medical measures. In February 1974 a barium meal examination showed active ulceration in an already scarred duodenal cap. A chest X-ray was normal.

On 24 February 1974 he underwent a truncal vagotomy and Finney type pyloroplasty through an upper midline abdominal incision. The vagus trunks were divided and haemostasis achieved without injury to the oesophageal muscle. He made an uneventful recovery.

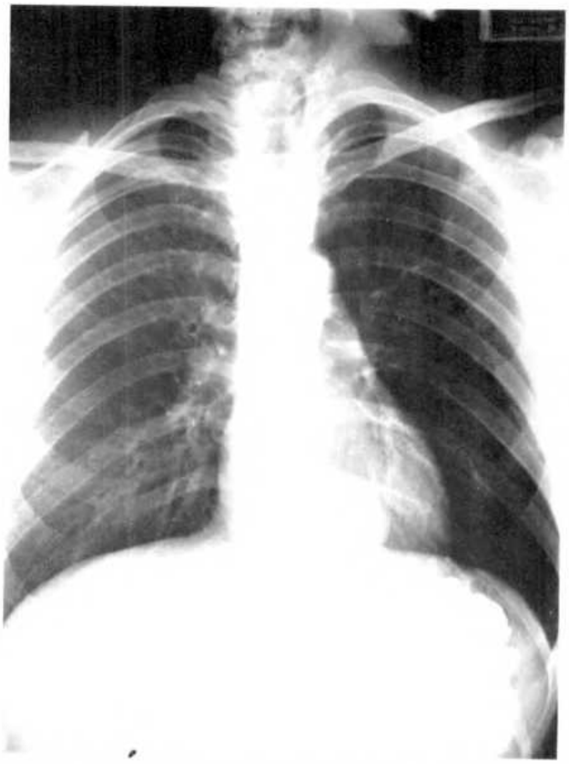


Fig. 1. Chest X-ray showing a smooth well-defined shadow lying medially at the left base.

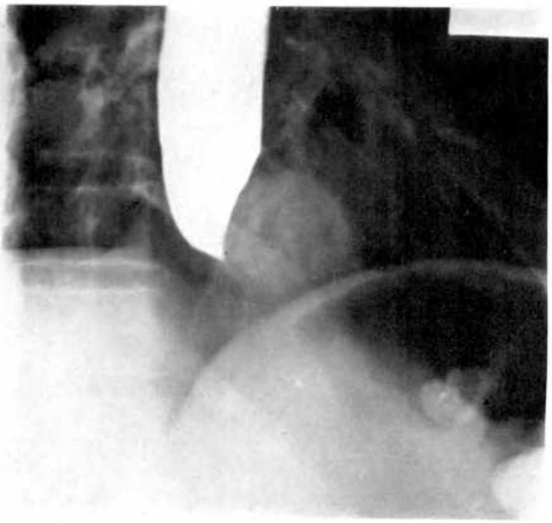


Fig. 2. Barium meal film showing the mass compressing the oesophagus at its lowest points.

On 14 March 1974 the patient was readmitted complaining of vomiting half an hour after meals. He indicated that food and fluid were sticking retrosternally. A chest X-ray (*Fig.* 1) revealed a shadow, smooth and well defined, lying medially at the left base. A barium swallow film (*Fig.* 2) showed that this mass was compressing the oesophagus at its lowest point. There was delay in the passage of barium through the obstruction, and the proximal oesophagus was dilated.

Initially treatment was conservative, the patient being fed intravenously. He underwent oesophagoscopy, and dilators passed to 27 F with ease on two separate occasions. Each time the mucosa was normal, but the relief obtained from bouginage proved to be temporary.

Seven weeks after his vagotomy and pyloroplasty another oesophagoscopy revealed complete obstruction of the lower oesophagus. The patient therefore underwent laparotomy through the previous upper midline abdominal incision. At the diaphragmatic hiatus the oesophagus, which otherwise was normal, was compressed by a mass of hard fibrous tissue. This mass completely surrounded, but appeared to be separate from, the oesophagus. A biopsy was taken, and the mass was dilated forcefully with the fingers to allow the oesophagus to re-expand. Biopsy of this material showed fibrous tissue with a few normal blood vessels. No evidence of starch granulomas was seen.

Recovery from this second operation was rapid and the patient left hospital after 8 days. When last seen 4 months after re-exploration the patient was symptom-free, and the radiological abnormalities could no longer be seen.

Discussion

The reported incidence of postvagotomy dysphagia differs widely, depending on the severity of the symptoms recorded. In a series of 1000 cases Wirthlin

---

* The Greenwich District Hospital and Miller General Wing, London.

and Malt (1972) found an incidence of dysphagia of 1 per cent after vagotomy. Williams and Cox (1969) cited a figure of 18 per cent in their series. Grimson et al. (1947) found that 33 per cent of patients complained of dysphagia if a transthoracic approach had been used for the vagotomy. It was noted by Dagradi et al. (1962) that a higher incidence of dysphagia could be found in the hands of certain surgeons who made a practice of searching for vagal nerve fibres in the oesophageal muscle.

Initially the cause of postvagotomy dysphagia was thought to be due to denervation of the sphincter mechanism of the lower oesophagus, and also to loss of normal peristalsis leading to a form of achalasia (Moses, 1947; Harris and Miller, 1960). Edwards (1970) showed by manometric and radiological studies of the oesophagus in patients with some dysphagia after vagotomy that the sphincter was intact and that peristalsis occurred normally. Carveth et al. (1962) attempted to denervate the lower oesophagus in dogs, and found that this could only be achieved by vagal nerve section at the level of the hila of the lungs.

Three cases have been described in the literature in which open operation has had to be carried out for complete obstruction of the lower oesophagus, some time after the original vagotomy. Bruce (1959) operated on a man with postvagotomy dysphagia. His symptoms started, as is often the case, 3 weeks after operation. After another 2 weeks he had developed complete obstruction, and was therefore fed by a jejunostomy. Oesophagoscopy revealed a normal oesophageal mucosa, but repeated bouginage failed to relieve the symptoms. The patient subsequently underwent a left thoracotomy, dense scar tissue being found to have surrounded the lower end of the oesophagus. This mass was adherent to the aorta, pre-vertebral fascia and the right lung. The lower oesophagus and this mass of scar tissue were excised and an oesophagogastric anastomosis carried out. Histology revealed a small but definite gap between the normal oesophagus and the fibrous tissue mass.

Guillory and Claggett (1967) described the finding of a dense ring of scar tissue surrounding the lower oesophagus in a case of postvagotomy dysphagia. This was partly excised and a modified Heller's procedure carried out. A left thoracotomy was the approach used in this case also. The third case was reported by Postlethwait et al. (1969) and was found to have a mass of fibrous tissue compressing the lower oesophagus. This mass of tissue was excised, using a left chest approach. The complete oesophageal obstruction was relieved in these 3 cases.

Comment

Postvagotomy dysphagia may appear some weeks after a seemingly successful truncal vagotomy. Usually the symptoms disappear spontaneously, and only occasionally is it necessary to resort to oesophagoscopy and dilatation. In just a few cases has a second operation been performed for oesophageal obstruction which had become complete.

From the evidence presented it would seem probable that the initial event in the production of postvagotomy dysphagia is haematoma formation around the lower end of the oesophagus. This eventually leads to peri-oesophageal fibrosis, causing compression of the lower oesophagus and very rarely complete obstruction.

The case we have described was one of the very few which did not respond to conservative measures, and it is of some interest that the mass causing oesophageal compression could be clearly seen on X-ray. The patient was not subjected to thoracotomy but to a lesser procedure, carried out through his original upper midline abdominal incision. This may have contributed to his rapid recovery, as may the fact that no direct attempt was made to dissect out the fibrous tissue mass which was compressing the lower end of the oesophagus.

Acknowledgement

I would like to thank Mr J. Candy for permission to publish details of this patient who was under his care.

References

BRUCE J. (1959) Dysphagia following vagotomy. *J. R. Coll. Surg. Edinb.* **4**, 170–178.

CARVETH S. W., SCHLEGEL J. F., CODE C. F. and ELLIS F. H. (1962) Esophageal motility after vagotomy, phrenicotomy, myotomy and myomectomy in dogs. *Surg. Gynecol. Obstet.* **114**, 31–42.

DAGRADI A. E., STEMPIEN S. J., SIRFER H. W. and WEINBERG J. A. (1962) Terminal esophageal spasm after vagotomy. *Arch. Surg.* **85**, 955–967.

EDWARDS D. A. W. (1970) Post vagotomy dysphagia. *Lancet* **2**, 90–92.

GRIMSON K. S., BAYLEN G. J., TAYLOR H. M., HESSER F. H. and RUNDLES R. W. (1947) Transthoracic vagotomy. *JAMA* **134**, 925–932.

GUILLORY J. R. and CLAGGETT O. T. (1967) Post vagotomy dysphagia. *Surg. Clin. North Am.* **47**, 833–839.

HARRIS J. and MILLER C. M. (1960) Cardiospasm following vagotomy. *Surgery* **47**, 568–570.

MOSES W. R. (1947) Critique on vagotomy. *New Engl. J. Med.* **237**, 603–610.

POSTLETHWAIT R. W., KIM S. K. and DILLON M. L. (1969) Esophageal complications of vagotomy. *Surg. Gynecol. Obstet.* **128**, 481–488.

WILLIAMS J. A. and COX A. G. (ed.) (1969) *After Vagotomy*. London, Butterworths.

WIRTHLIN L. S. and MALT R. A. (1972) Accidents of vagotomy. *Surg. Gynecol. Obstet.* **135**, 913–916.

Br. J. Surg. Vol. 62 (1975) 356–359

The relationship of anaemia to gastric secretion more than 15 years after vagotomy and gastro-enterostomy

E. J. WHELDON, C. W. VENABLES AND IVAN D. A. JOHNSTON*

SUMMARY

Iron deficiency anaemia is common following vagotomy and gastro-enterostomy, and this study has shown that all the anaemic patients had low gastric secretion.

After correction of their anaemia, gastric secretion was increased, but was still very low, and when these levels were compared with secretion in fit non-anaemic patients it was found that the latter group had a significantly higher secretion, and that a high proportion of them showed evidence of incomplete vagotomy.

These results suggest that there is a relationship between the levels of gastric secretion in patients after vagotomy and gastro-enterostomy and the development of anaemia. It may be that inadequate gastric secretion impairs the release of elemental iron from the diet and its subsequent absorption.

PARTIAL gastrectomy, whether Polya or Billroth I, is known to be associated with a high incidence of anaemia developing a number of years after operation. This anaemia has been shown to be mainly due to iron deficiency (Hobbs, 1961). The incidence of anaemia varies widely (from 10 to 80 per cent) in different series, and Deller et al. (1962) calculated an average of 28 per cent from 33 reports. Macrocytic anaemia was reported by these workers in only 1·5 per cent of patients, but Jones et al. (1962) reported an incidence of 16 per cent. A study carried out by Mollin and Hines in 1964 found serum vitamin B_{12} and folic acid deficiencies in more than 25 per cent of their patients.

There has been a great deal of investigation into the possible causes of the iron deficiency anaemia following partial gastrectomy. Little evidence has been produced to indicate that these patients take an inadequate amount of iron in their diets. It would seem possible, therefore, that the anaemia might be caused by impaired absorption. It has been suggested by Stevens et al. (1959) that patients after partial gastrectomy are unable to increase dietary iron absorption in the presence of iron deficiency anaemia, whereas iron deficient patients who have not had gastric surgery are able to do so. Other workers have shown that absorption of both ferrous and ferric salts in anaemic patients after gastrectomy is as good as in anaemic patients who have not undergone surgery (Baird and Wilson, 1959). It would appear that postgastrectomy patients might have a limited ability to break down the protein complex of dietary iron, and it has been suggested that gastric secretion facilitates this breakdown (Goldberg et al., 1963; Jacobs et al., 1966).

All this work was carried out on patients following partial gastrectomy, and it was felt that loss of the gastric reservoir and glandular tissue might be responsible for the development of nutritional disturbances. It was hoped that with vagotomy and drainage these problems would not arise. Unfortunately, several workers have shown that a similar incidence of anaemia occurs following this operation (Burge and Pick, 1958; Cox et al., 1964).

A recent study of 230 patients who had undergone vagotomy and gastro-enterostomy more than 15 years previously (Wheldon et al., 1970) showed that this operation was associated with a high incidence of iron deficiency anaemia (30 per cent). There was no evidence of macrocytosis in any of the patients, and serum vitamin B_{12} levels were all within the normal range. When these patients were reviewed at 10 years after surgery (Feggetter and Pringle, 1963), the incidence of iron deficiency anaemia was 10 per cent. Anaemia after vagotomy and drainage develops later and is less severe than that recorded after gastrectomy (Jones et al., 1962).

It would appear that alteration in gastric secretion might play an important role in the development of iron deficiency anaemia, and a study was designed to investigate this.

Table I: DETAILS OF THE TWO GROUPS IN THE PRESENT STUDY

	Anaemic group ($n = 12$)	Non-anaemic group ($n = 11$)
Age (yr)	55·8± 8·4	55·6±5·9
Weight (kg)	60·2±10·3	68·5±6·2
Haemoglobin (g/100 ml)	8·5± 1·1	14·6±0·6
Time since vagotomy (yr)	17·1± 1·6	17·5±1·7
Length of history before vagotomy (yr)	8·2± 6·5	6·8±3·0

All results given as mean ±s.d.

Patients and methods

Twenty-three patients were investigated (*Table I*). Twelve had haemoglobin levels below 10 g/100 ml (70 per cent) at the time of their review and their mean level was 8·4 g/100 ml (58·9 per cent). There was no obvious cause of anaemia in these patients, e.g. haemorrhoids, positive occult blood or any obvious disease associated with anaemia. A dietician calculated the mean daily iron intake of each patient,

---

* Department of Surgery, University of Newcastle upon Tyne, Royal Victoria Infirmary, Newcastle upon Tyne.

and all the patients took more than the minimum daily requirement of 10 mg, the mean being 16·1 mg.

The remaining 11 patients were selected because at the time of their review they were completely well and had normal haemoglobin levels (mean value 14·6 g/100 ml). The two groups were comparable for age, length of history before operation and length of follow-up.

There was a difference in the mean weights of the two groups: 68·5 kg in the non-anaemic patients and 60·2 kg in the anaemic patients. This was partly explained by the fact that there were 2 women in the anaemic group, and there were no women of comparable status in the non-anaemic group. The actual weights of the patients in this study were compared with their standard weights calculated from their age, sex and height (Kemsley et al., 1962). There was no significant difference between their actual and standard weights in the two groups. There was no alteration in the weights of the anaemic patients after correction of their anaemia. Haemoglobin was estimated by the cyanmethaemoglobin method, and serum iron by AutoAnalyzer.

The acid and pepsin secretory response to pentagastrin (6·0 µg/kg i.m.) and to insulin (0·2 u./kg i.v.) was assessed in all the patients either by separate tests or by a combined pentagastrin/insulin test (Venables, 1972). Gastric secretion was collected by a 'washout' technique in all but one patient; this technique allowed an estimate of uncollected secretion to be made. Acid was measured as total titratable acidity to pH 7·0 using an automatic titrimeter (Radiometer), and pepsin was measured as total peptic activity at pH 2·1 using a modification of Hunt's (1948) technique with albumin (Fr. V) as substrate and expressing results as equivalent to the peptic activity produced by a known amount of crystalline pepsin (Sigma 1 : 60 000). The outputs of acid and pepsin were calculated for the hour after pentagastrin stimulation and the peak 30-minute output after insulin.

As it could be argued that any secretory changes found were due to the presence of anaemia (Stone, 1968), the anaemia was corrected by the administration of oral ferrous gluconate 200 mg three times daily. At the end of 3 months' treatment the mean haemoglobin had risen from 58·9 to 95·3 per cent, and the serum iron from 31·5 µg/100 ml to 96·8 µg/100 ml. Repeat pentagastrin tests were carried out at this time.

Results

Estimation of acid and pepsin secretion before correction of the anaemia (*Fig.* 1) revealed that only 2 patients had acid outputs of more than 1 mEq/h and the mean output was only 0·6 mEq/h. Pepsin output was also markedly reduced, as 3 patients had no measurable pepsin response and the highest output was only 23·4 mg/h with a mean of 8·2 mg/h.

Three months later, after correction of the anaemia, there was a significant increase in the gastric secretion ($P<0{\cdot}01$). All but 2 patients had an increase in both acid and pepsin output. Six patients now had acid outputs of more than 1 mEq/h, but the mean response was still low at only 1·55 mEq/h. Pepsin output showed a threefold rise from a mean of 8·2 to 27·3 mg/h.

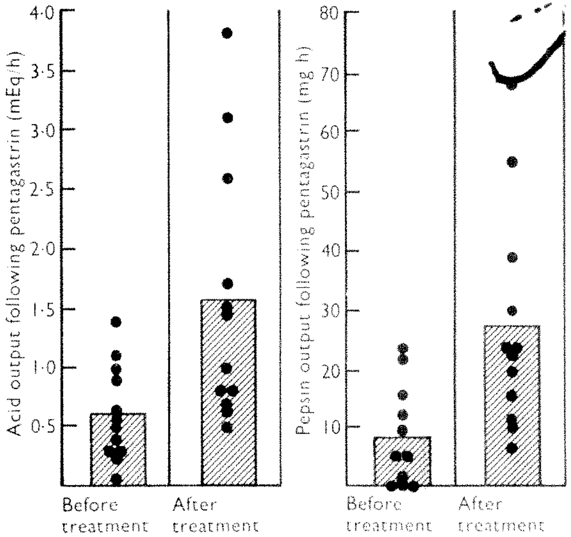


Fig. 1. Effects of correction of anaemia on gastric secretion. Acid output, $P<0{\cdot}01$ (u. = 25·5). Pepsin output, $P<0{\cdot}001$ (u. = 18·5).

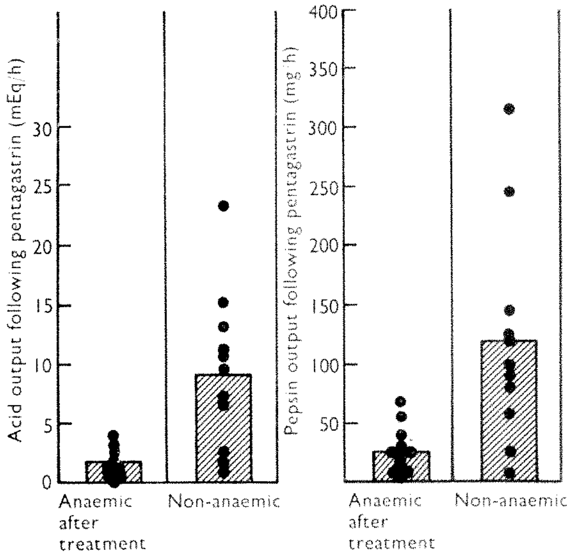


Fig. 2. Comparison of the gastric secretion of anaemic and non-anaemic patients. Acid output, $P<0{\cdot}001$ (u. = 9·5). Pepsin output, $P<0{\cdot}001$ (u. = 14).

The results obtained after correction of the anaemia were compared with those obtained in our non-anaemic group (*Fig.* 2). Only 3 of the non-anaemic patients showed acid outputs similar to those of the anaemic group and one of these had not had a 'washout' pentagastrin test so that the secretory response was probably an underestimate. The mean acid output in the non-anaemic group was 9·2 mEq/h and the pepsin output was 119·3 mg/h. These differences are highly significant ($P<0{\cdot}001$).

Table II: ASSESSMENT OF COMPLETENESS OF VAGOTOMY IN THE NON-ANAEMIC PATIENTS

Test	No. of patients
Hollander	
>20 mEq/l (positive)	9
<20 mEq/l (negative)	2
Insulin: pentagastrin acid ratio	
>45%	4
<45%	7

An attempt was made to assess the completeness of vagotomy in all the patients studied. This was done in two ways: either by the rise in acid concentration of more than 20 mEq/l after insulin stimulation (Hollander, 1946) or by an acid ratio of more than 45 per cent, calculated from the acid output response to insulin and pentagastrin (Venables, 1972). In the anaemic patients it was difficult to assess the completeness of vagotomy by either technique, as the acid outputs were so low. It was not possible, therefore, to say with certainty whether this low response was due to complete vagal section or to loss of secretory cells. Of the non-anaemic group (*Table II*), 9 showed a rise in acid concentration of more than 20 mEq/l, thus fulfilling Hollander's criteria for incomplete vagotomy, and 4 of these had acid ratios of more than 45 per cent, suggesting that the vagotomy was definitely incomplete.

Discussion

In our earlier study of patients who had undergone vagotomy and gastro-enterostomy more than 15 years previously (Wheldon et al., 1970) it was shown that iron deficiency anaemia was almost as common as that reported after gastrectomy. This was disappointing as it had been hoped that preservation of the gastric reservoir function of the stomach would prevent this complication.

One possible cause for this anaemia was a reduced iron intake, but dietary analysis failed to demonstrate this, supporting the findings of others (Pulvertaft and Cox, 1969).

Another mechanism could have been the bypassing of the duodenum in these patients, as Wallenstein (1958) suggested that this would reduce absorption from the duodenum and proximal jejunum. However, all our anaemic patients responded rapidly to oral ferrous gluconate, suggesting that this was not true for elemental iron.

Jacobs et al. (1966) have demonstrated that gastric secretion facilitates iron absorption. As dietary iron is not normally in its elemental form but bound to protein as an iron–protein complex, it is possible that the anaemia could be related to an inability to split this complex due to an effect of the operation upon gastric secretion. The present study was designed to investigate this possibility.

Because it might be argued that any secretory changes we found in our anaemic patients were due to the anaemia and not the cause of it, we repeated our secretory tests following correction of the iron deficiency and were able to confirm the findings of Stone (1968) that secretion of both acid and pepsin rose significantly after correction of the anaemia. However, even this increased secretory response was far lower than that found in our non-anaemic group.

Goldberg et al. (1963) suggested that 'acid' alone facilitated iron absorption, but Hines et al. (1967) felt that pepsin secretion was more important as this was capable of splitting the food iron–protein complex when activated by a fall in pH. Koepke and Stewart (1964) suggested that there was a factor present in gastric juice, similar to intrinsic factor, that enhanced iron absorption.

Whichever of the above possibilities is correct, it is likely that vagotomy will alter their roles as it results in a reduction of *all* gastric juice constituents.

Another possible cause for the reduction in gastric secretion found in our anaemic patients has been suggested by Williams (1964). He has postulated that the duodenal and bile juice reflux associated with a gastro-enterostomy may result in chronic gastritis, glandular atrophy and subsequent hyposecretion. Such a suggestion would explain why anaemia is less common after pyloroplasty where reflux is less (Wastell, 1969). It is of interest to note how many of our non-anaemic group had evidence of residual vagal function on insulin testing. This capacity to secrete acid may have protected the stomach from the effects of the reflux of alkaline secretion, and this in turn may have prevented mucosal atrophy.

Finally, it could be suggested that the increased rate of gastric emptying found after vagotomy and drainage (Owren, 1953; McKelvey, 1970) prevented the adequate mixing of gastric juice and food, reducing the liberation of elemental iron from the food while it was in contact with the iron-absorbing area of the small intestine. Incomplete vagotomy, even though it maintains a higher level of gastric secretion, cannot be the only factor, as several non-anaemic patients had no evidence of residual vagal function after insulin stimulation.

Acknowledgements

We wish to thank Professor A. L. Latner and the Department of Clinical Biochemistry, University of Newcastle upon Tyne, for their assistance with this study, Staff Nurse M. Curd for performing many of the secretory studies, Mrs M. Foster for her secretarial assistance and the members of the Department of Surgery for their assistance throughout the study.

References

BAIRD I. MCL. and WILSON G. M. (1959) The pathogenesis of anaemia after partial gastrectomy. *Q. J. Med.* **28**, 21–41.

BURGE H. and PICK E. J. (1959) Long term results of vagotomy and gastroenterostomy in chronic duodenal ulceration. *Br. Med. J.* **1**, 613–615.

COX A. G., BOND M. R., PODMORE D. A. and ROBB D. P. (1964) Aspects of nutrition after vagotomy and gastrojejunostomy. *Br. Med. J.* **1**, 465–469.

DELLER D. J., RICHARDS W. C. D. and WITTS L. J. (1962) Changes in the blood after partial gastrectomy with special reference to vitamin B_{12}. *Q. J. Med.* **31**, 89–102.

FEGGETTER G. Y. and PRINGLE R. (1963) Long-term results of bilateral vagotomy and gastrojejunostomy for chronic duodenal ulcer. *Surg. Gynecol. Obstet.* **116**, 175–179.

GOLDBERG A., LOCHEAD A. C. and DAGG J. H. (1963) Histamine-fast achlorhydria and iron absorption. *Lancet* **1**, 848–850.

HINES J. D., HOFFBRAND A. V. and MOLLIN D. L. (1967) The hematologic complications following partial gastrectomy. *Am. J. Med.* **43**, 555–569.

HOBBS J. R. (1961) Iron deficiency after partial gastrectomy. *Gut* **2**, 141–149.

HOLLANDER F. (1946) The insulin test for presence of intact nerve fibres after vagal operations for peptic ulcer. *Gastroenterology* **7**, 607–614.

HUNT J. N. (1948) A method of estimating peptic activity in gastric contents. *J. Biochem.* **42**, 104–109.

JACOBS A., RHODES J., PETERS D. K., CAMPBELL H. and ESKINS J. D. (1966) Gastric acidity and iron absorption. *Br. J. Haematol.* **12**, 728–736.

JONES C. T., WILLIAMS J. A., COX E. V., MEYNELL M. J., COOKE W. T. and STAMMERS F. A. R. (1962) Peptic ulceration. Some haematological and metabolic consequences of gastric surgery. *Lancet* **2**, 425–428.

KEMSLEY W. F. F., BILLEWICZ W. Z. and THOMSON A. M. (1962). A new weight-for-height standard based on British anthropometric data. *Br. J. Prev. Soc. Med.* **16**, 189–195.

KOEPKE J. A. and STEWART W. B. (1964) Role of gastric secretion in iron absorption. *Proc. Soc. Exp. Biol. Med.* **115**, 927–929.

MCKELVEY S. T. D. (1970) Gastric incontinence and post-vagotomy diarrhoea. *Br. J. Surg.* **57**, 741–747.

MOLLIN D. L. and HINES J. D. (1964) Observations on the nature and pathogenesis of anaemia following partial gastrectomy. *Proc. R. Soc. Med.* **57**, 575–580.

OWREN P. A. (1953) The pathogenesis and treatment of iron deficiency anaemia after partial gastrectomy. *Acta Chir. Scand.* **104**, 206–214.

PULVERTAFT C. N. and COX A. G. (1969) Effects of vagotomy on haemopoiesis. In: WILLIAMS A. J. and COX A. G. (ed.) *After Vagotomy*. London, Butterworths, pp. 150–156.

STEVENS M. D., PIRZIO-BIROLI G., HARKINS H. N., NYHUS L. M. and FINCH C. A. (1959) Iron metabolism in patients after partial gastrectomy. *Ann. Surg.* **149**, 534–538.

STONE J. R. (1968) Gastric secretory response to iron therapy. *Gut* **9**, 99–105.

VENABLES C. W. (1972) An assessment of the value of measuring uncollected gastric secretion during routine secretion studies in man. *Br. J. Surg.* **59**, 473–477.

WALLENSTEIN S. (1958) Iron absorption after Bilroth I and II partial gastrectomy. *Acta Chir. Scand.* **115**, 270–275.

WASTELL C. (1969) Long-term clinical and metabolic effects of vagotomy with either gastrojejunostomy or pyloroplasty. *Ann. R. Coll. Surg. Engl.* **45**, 193–211

WHELDON E. J., VENABLES C. W. and JOHNSTON I. D. A. (1970) Late metabolic sequelae of vagotomy and gastroenterostomy. *Lancet* **1**, 437–440.

WILLIAMS J. A. (1964). Effects of upper gastro-intestinal surgery on blood formation and bone metabolism. *Br. J. Surg.* **51**, 125–135.

Br. J. Surg. Vol. 62 (1975) 360–363

Pancreatic pseudocysts in children: 4 cases from Uganda

J. WILSON CARSWELL, J. COTTER AND S. P. MASTER*

SUMMARY

Four cases of pancreatic pseudocyst in African children are described. There is some evidence that they followed pancreatitis of unknown aetiology. None had a history of trauma. Three were treated by cystogastrostomy, and the fourth by excision of the cyst.

PSEUDOCYSTS of the pancreas are not commonly seen in children (Mustard et al., 1969). Up until 1968 about 50 cases in children had been described in the literature. Sixty per cent of the cases are said to follow blunt abdominal trauma, 29 per cent to follow pancreatitis and 11 per cent to form a miscellaneous group, following such diseases as mumps and gallstones (Mustard et al., 1969). Typically the child presents with upper abdominal pain, nausea, vomiting, anorexia and weight loss. There may be a history suggestive of trauma or pancreatitis within the preceding 3 months. An epigastric mass is present although initially it may be masked by ascites. This mass is usually a tender unilocular cyst containing a litre or so of fluid. The pseudocyst displaces the adjacent organs, and this can be confirmed by X-ray examination. The serum amylase level is usually raised.

Untreated cysts may bleed, become infected or rupture, causing peritonitis. It will rarely disappear spontaneously. For these reasons surgery is usually recommended. In recent years cystogastrostomy and excision of the cyst have been the most commonly used procedures.

Four pancreatic pseudocysts seen in children in Kampala, Uganda, are described.

Case reports

Case 1: A 2-year-old Muganda boy, weighing 9·5 kg on admission, had been unwell for some months and had not been gaining weight. For 3 months his abdomen had been gradually distending, and in the month before admission his feet had started to swell. There was no history of abdominal trauma.

On admission he was wasted and anaemic and in a poor state of nutrition. There was gross abdominal distension, with ascites and prominent veins on the anterior abdominal wall. There was oedema of both feet. His skin was pale and his hair brown and brittle. For these reasons a clinical diagnosis of kwashiorkor was made. No abdominal mass was palpable. The child developed diarrhoea, but gradually improved with supportive therapy.

Investigations revealed the following: haemoglobin 6·7 g per cent, serum proteins 5·8 g per cent (mean), serum bilirubin <0·5 mg/100 ml, serum alkaline phosphatase 37 i.u./100 ml, prothrombin time 18 seconds (control 14 seconds), urine normal.

On tapping the abdomen straw-coloured ascitic fluid was withdrawn. The ascites was treated by paracentesis and diuretics, and gradually decreased. The haemoglobin was raised by whole blood transfusion on two occasions, and vitamin K was given to correct the prothrombin level. As the ascites decreased a mass, measuring about 7 × 10 cm, was felt in the left upper abdomen. At this point the possibility of an intra-abdominal malignancy was raised. A barium enema examination at this time showed downward displacement of the transverse colon.

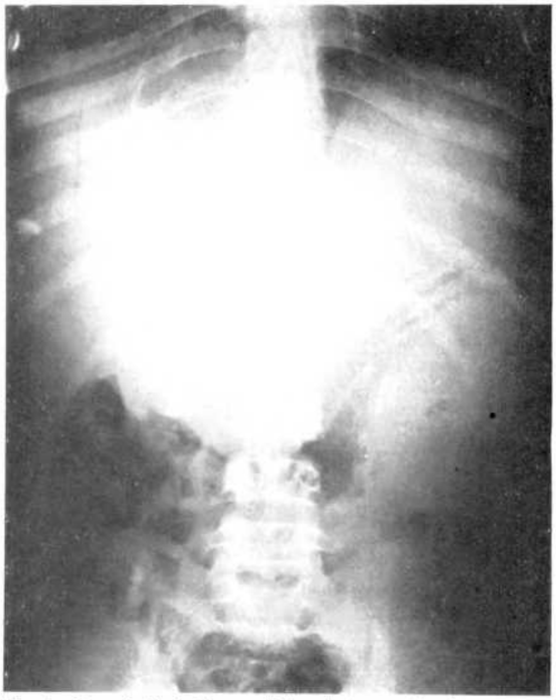


Fig. 1. *Case* 2. Plain X-ray of the abdomen showing pancreatic calcification.

As the cause of the ascites was not established a laparotomy was carried out. A pancreatic pseudocyst was present arising from the body of the pancreas. It was unilocular and contained nearly a litre of fluid. It pushed the stomach forwards and upwards, and the transverse colon downwards. A posterior cystogastrostomy was carried out. The child made a slow but uneventful recovery and was discharged 3 weeks later.

Case 2: A 12-year-old Munyoro boy was well until 5 months before admission. He had gradually developed abdominal pain, usually generalized, but occasionally radiating through to the back. It was sometimes colicky in nature. He also had had occasional episodes of diarrhoea.

In the week before admission he had had constant severe abdominal pain associated with anorexia, vomiting and loss of weight. There was no history of trauma. An upper abdominal swelling had been noticed by the patient for 3 weeks before admission. It was present in the epigastrium and extended to both hypochondria.

---

* Mulago and Nsambya Hospitals, Kampala, Uganda.
Present address of S. P. Master: Royal Victoria Hospital, Halifax, Nova Scotia.

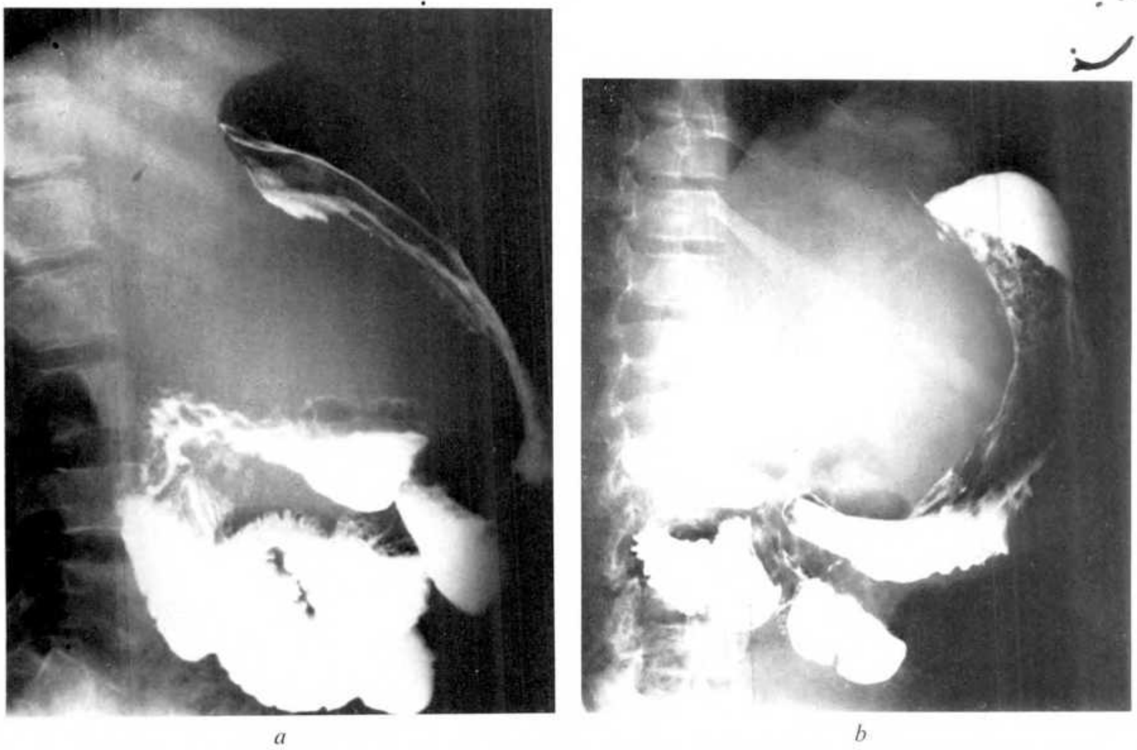


Fig. 2. *Case* 2. Barium meal films showing anterior displacement of the stomach (*a*) anteriorly and (*b*) to the left and a curved impression in the lesser curvature.

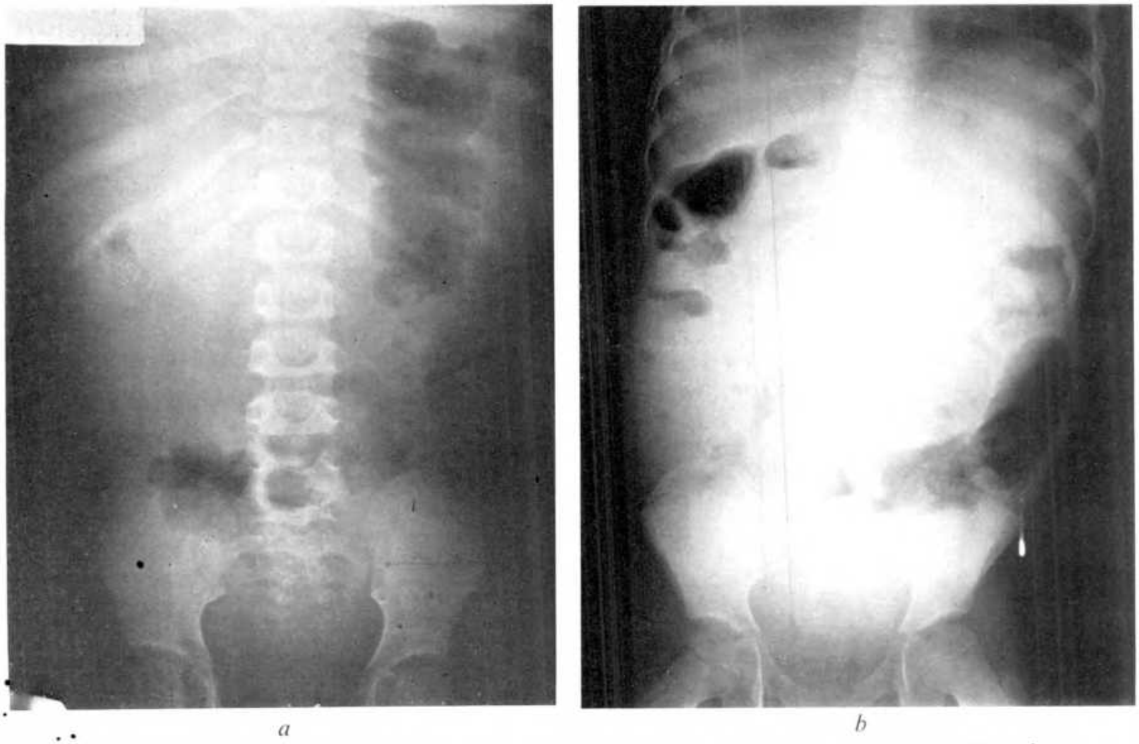


Fig. 3. *Case* 3. Plain X-rays of the abdomen showing displacement of the stomach upwards and of the transverse colon downwards.

On examination the patient was wasted. He had a large tender mass in the epigastrium and dilated veins in the upper abdomen. The spleen was enlarged. There was no ascites.

Investigations revealed the following: haemoglobin 13·6 g per cent, serum proteins 7·1 g per cent, serum bilirubin 0·5 mg/100 ml, serum alkaline phosphatase 97 i.u./100 ml, α-fetoprotein negative, serum amylase 800 Somogyi units/100 ml, WBC 5600/mm^3. A plain X-ray of the abdomen showed pancreatic calcification (*Fig.* 1). A barium meal examination showed displacement of the stomach forwards and to the left (*Fig.* 2).

A laparotomy was carried out. There was a large unilocular pancreatic pseudocyst containing a litre of bloodstained fluid. The cyst presented in the lesser sac and was pushing the stomach forwards. A posterior cystogastrostomy was fashioned. The child made an uneventful recovery. A postoperative glucose tolerance curve was normal. When seen at follow-up 3 months later the patient was in good health.

Case 3: A 5-year-old Muganda girl, weighing 16 kg on admission, had had a febrile illness, diagnosed by the mother as measles, a month before admission. A few weeks after this she had gradually developed abdominal pain. She was constipated, but had not vomited. She also had backache. There was no history of trauma.

On admission to hospital the patient was in a fair general condition. She was afebrile. Her abdomen was uniformly distended, and there was some ascites. There was a large tender swelling in the left hypochondrium extending to the epigastrium.

Investigations revealed the following: haemoglobin 7·9 g per cent, serum proteins 7·4 g/100 ml, serum bilirubin 0·5 mg/100 ml, serum alkaline phosphatase 85 i.u./100 ml, serum amylase on 25 October 1971, 274 Somogyi units/100 ml, and on 2 November, 415 Somogyi units/100 ml, blood urea 30 mg/100 ml. Specimens of stool contained no parasites. A plain X-ray of the abdomen showed an upper abdominal mass with displacement of the stomach upwards and the transverse colon downwards (*Fig.* 3). A barium meal study confirmed this.

The anaemia was corrected by whole blood transfusion. At laparotomy there was a unilocular pseudocyst, measuring 22×22 cm, of the body of the pancreas in the lesser sac pushing the stomach forwards. It contained about 2 litres of fluid. A posterior cystogastrostomy was fashioned with a 5-cm diameter stoma. A biopsy was taken which showed changes compatible with a pseudocyst of the pancreas. The patient made an uneventful recovery. A postoperative barium meal examination showed no reflux through the stoma.

Case: 4: A 9-year-old Munyarwanda boy had been ill for 8 months. He had abdominal pain, abdominal distension and anorexia and weighed 18 kg on admission. There was no history of abdominal trauma.

On admission the patient was in a poor general state. He was thought initially to have ascites, but on further examination the swelling was found to be due to a large central abdominal cyst. The cyst had a fluid thrill and extended into the left loin. It did not move on respiration. There was no ankle oedema or ascites.

Investigations revealed the following: haemoglobin 10·4 g per cent, serum proteins 7·4 g/100 ml, serum amylase 120 Somogyi units/100 ml, blood urea 28 mg/100 ml, prothrombin time 14 seconds (control 12 seconds), WBC 10 000/mm^3, ESR 99 ml/h. Examination of a stool showed no excess fat present. The urine revealed no glycosuria.

It was felt that pancreatic pseudocyst was a likely diagnosis, and the patient was prepared for operation. The abdomen was opened by a transverse supra-umbilical incision. A large cyst was present filling most of the abdomen. It pushed the stomach upwards and the transverse colon downwards. It arose from the distal part of the body of the pancreas from an area about 4 cm across. The cyst was dissected free and was removed intact. It weighed 3·6 kg and had an amylase content of 180 Somogyi units/100 ml. There was a bare area of the distal part of the body of the pancreas present at the end of the operation. The abdomen was not drained. Because of the possibility of postoperative pancreatitis, the patient was given probanthine postoperatively. The child made an uneventful recovery and was discharged 13 days after operation.

Histology confirmed the diagnosis of pancreatic pseudocyst. The child was seen 3 months after operation. He was in good health and had gained weight.

Diagnosis

The presentation of these cases did not differ significantly from that described in children elsewhere. Abdominal pain was the presenting symptom in *Cases* 2, 3 and 4, while failure to thrive was the main complaint in *Case* 1. Three of the children (*Cases* 1, 2 and 4) weighed less than expected for their ages. In 3 instances an epigastric mass was palpable on admission, and in the fourth (*Case* 1) the mass became palpable after paracentesis.

The serum amylase level was not very helpful in the diagnosis of this condition. It was raised in *Cases* 2 and 3 and was normal in *Case* 4, normal values in Ugandan African adults being 209 ± 63 Somogyi units/100 ml (Mugondi, 1971). A plain X-ray of the abdomen was found useful. All the cases showed the presence of an epigastric mass or opacity with displacement of the stomach. *Case* 2 also showed pancreatic calcification. Barium studies confirmed the stomach displacement. In *Case* 2 the stomach was displaced anteriorly and to the left, and in *Case* 1 the transverse colon was displaced downwards.

Treatment

Case 1 was in a poor nutritional state and required extensive preoperative preparation including blood transfusion and vitamin K. Apart from this no specific preoperative therapy was required. Three of the 4 cases were treated in a similar manner. As soon as the patient was fit, an exploratory laparotomy was carried out during which the diagnosis was established. A posterior cystogastrostomy was carried out. Owing to the relatively dense adherence of the cyst wall to the stomach in all 3 cases this was a straightforward procedure and caused no technical difficulties. Theoretically this may be followed by reflux of gastric contents into the pseudocyst. This may then cause bleeding or reactivation of the pancreatitis. However, this did not occur in any of the cases described here. A barium meal film taken 3 weeks postoperatively in *Case* 3 showed normal stomach appearances with no evidence of reflux into the cyst.

Case 4 had a simple excision of the cyst with no untoward complications.

Comment

It has been reported that the commonest cause of pancreatic pseudocyst in children is pancreatitis following blunt abdominal trauma (Mustard et al., 1969), but many of these cases came from North America. In none of the cases presented here was there such a history. Although pancreatitis is not common in children it does occur, and cases of pancreatitis in African children have been described by Collins (1958) and Owor (1972). Adults in Uganda not infrequently suffer from pancreatitis, which may proceed to pancreatic calcification and diabetes mellitus. It is presumed that a preceding pancreatitis was responsible for the pancreatic calcification seen radiologically in *Case* 2.

Of new diabetic patients presenting at Mulago Hospital, 7·6 per cent have radiological pancreatic calcification, without evidence of active pancreatitis (Shaper, 1964). In the present series, however, *Case* 2 had a normal glucose tolerance curve postoperatively, and there was no evidence of diabetes mellitus.

Even if it is assumed that there was a preceding pancreatitis in these children the aetiology of the pancreatitis is open to speculation. The onset of the disease in *Case* 2 was related to a febrile illness diagnosed by the mother as measles. This may be no more than coincidental and may have been some other viral disease. Cases of pancreatic pseudocyst have followed other viral diseases such as mumps (Oeconomopoulos and Lee, 1960) and Coxsackie virus (Veghelyi, 1950).

Case 1 also had some interesting features preceding the appearance of the pseudocyst. On admission he had many of the signs of kwashiorkor. Cases of pancreatic pseudocyst following kwashiorkor pancreatitis have been described (Udekwu et al., 1965), but they are uncommon. Many cases of kwashiorkor are seen in Kampala, but pancreatitis is not a common complication among these patients. The pancreatic changes in kwashiorkor are usually in the direction of atrophy (Davies, 1948) and reduction in pancreatic digestive enzymes (Thompson and Trowell, 1952). These two factors would appear to make pancreatitis less likely to occur in children with kwashiorkor.

Chronic pancreatic disease is a major cause of malabsorption in adults in Uganda (Banwell et al., 1967), and *Case* 1 may have been suffering initially from chronic pancreatic disease. The resulting malabsorption would produce some of the clinical features of kwashiorkor or congestive heart failure or cirrhosis. There was, however, no radiological evidence of malabsorption. None of the children had biliary disease or a history of alcoholic ingestion.

There are several points which are perhaps worth making. Pancreatic pseudocyst may be commoner than generally believed among children in tropical Africa. It may present in such children as an ascites of unknown origin (Hendren, 1965). The serum amylase may not be greatly elevated in this condition.

Aetiologically, the factors precipitating the possible initial pancreatitis in these children are not clear. The role played by viruses and malnutrition may be important.

References

BANWELL J. G., HUTT M. J. R., LEONARD P. J., BLACKMAN V., CONNOR D. W., MARSDEN, P. D. and CAMPBELL J. (1967) Exocrine pancreatic disease and the malabsorption syndrome in tropical Africa. *Gut* **8**, 388–401.

COLLINS J. (1958) Pancreatitis in young children. *Arch. Dis. Child.* **33**, 432–436.

DAVIES J. N. P. (1948) The essential pathology of kwashiorkor. *Lancet* **1**, 317–320.

HENDREN W. H., GREEP J. M. and PATTON A. S. (1963) Pancreatitis in childhood: experience with 15 cases. *Arch. Dis. Child.* **40**, 132–145.

MUGONDI S. C. (1971) Serum amylase in Ugandan Africans. *Makerere Med. J.* **16**, 30–31.

MUSTARD W. T., RAVITCH M. M., SNYDER W. H., WELCH N. J. and BENSON C. O. (1969) *Paediatric Surgery*, 2nd ed., vol. 1. Chicago, Year Book, pp. 755–757.

OECONOMOPOULOS C. T. and LEE M. J. jun. (1960) Pseudo-cysts of the pancreas in infants and young children. *Surgery* **47**, 836–845.

OWOR R. (1972) Chronic pancreatic disease in African children. *Uganda Med. J.* **1**, 7–9.

SHAPER A. G. (1964) Aetiology of chronic pancreatic fibrosis with calcification seen in Uganda. *Br. Med. J.* **1**, 1607–1609.

THOMPSON M. D. and TROWELL H. C. (1952) Pancreatic enzyme activity in duodenal contents of children with a type of kwashiorkor. *Lancet* **1**, 1031–1035.

UDEKWU F., NWANKONOBI F. and FRANCIS T. I. (1965) Pancreatic pseudo-cysts in children. *J. Int. Coll. Surg.* **44**, 123–127.

VEGHELYI P. V. (1950) Nutritional oedema. *Ann. Paediatr.* (*Basel*) **175**, 349–377.

Br. J. Surg. Vol. 62 (1975) 364–372

Diagnosis, clinical course and treatment of acute dermal gangrene

I. McA. LEDINGHAM AND M. A. TEHRANI*

SUMMARY

Twenty patients with acute dermal gangrene following surgery, trauma or sepsis are described. In 12 the skin became gangrenous secondary to a necrotizing process affecting the subdermal fascia, and in 8 the condition arose primarily in the skin. In the first group mortality was high unless radical excision of the necrotic fascia was performed at an early stage; in 3 of the recent patients the overlying skin was removed, defatted and stored for later grafting. In the second group, incision and adequate drainage combined with antibiotics seemed to suffice. Hyperbaric oxygen was of dubious value in the first group but appeared to contribute to arrest of the lesion in the second group.

ACUTE dermal gangrene, although relatively rare in modern surgical practice, can be very alarming. The rarity of the condition not infrequently causes delay in diagnosis and treatment, with the result that the mortality remains high. The multiplicity of terms used to describe variants of the condition further complicates understanding of the clinical problem (Meleney 1933; Crosthwait et al., 1964).

With the advent of hyperbaric oxygen therapy, centres possessing hyperbaric facilities have tended to attract patients with various types of dermal gangrene on the basis that hypoxia and infection contribute to the progressive nature of the condition. Over the past 9 years a number of such patients have been referred to the Hyperbaric Unit at the Western Infirmary, Glasgow, and it is the purpose of this paper to present the accumulated clinical experience and to analyse the possible therapeutic implications, including the role of hyperbaric oxygen.

The confusing terminology which exists in the current literature prompted the authors to simplify the classification of these conditions into two categories. Thus, the term 'necrotizing fasciitis' (Wilson, 1952) has been used to describe a progressive, usually rapid, necrotizing process affecting the subcutaneous fat, the superficial fascia and the superior surface of the deep fascia. The skin is initially intact but becomes gangrenous secondary to interruption of its deep blood supply. 'Progressive bacterial gangrene' describes a more slowly progressive lesion affecting the total thickness of skin but not involving deep fascia; pus formation is variable. In the patients of both categories almost all the lesions followed wounds or sepsis of the abdominal wall or perineum, although in some cases there was extensive spread to involve other areas of the body. No patient in whom bacteriological culture revealed a predominant growth of clostridial organisms was included.

Patients and methods

The period of study extended from 1965 to 1974. Twenty patients were included in the series. Twelve were suffering from necrotizing fasciitis and 8 from progressive bacterial gangrene. Fourteen patients were referred from various parts of the United Kingdom and the remainder were from the surgical units of the Western Infirmary.

The bacteriological, haematological and pathological laboratories were extensively used in the investigation and assessment of treatment of these patients. Medical and surgical care varied with the nature of the underlying disease process but most patients received hyperbaric oxygen at some stage of their illness. The general condition of several of the patients was serious enough to necessitate care in the Intensive Therapy Unit of the hospital (after 1967). Prolonged rehabilitation was required in a few of the survivors and it was the usual practice for this phase of the patient's care to be conducted by the referring clinician.

Clinical course, investigations and treatment

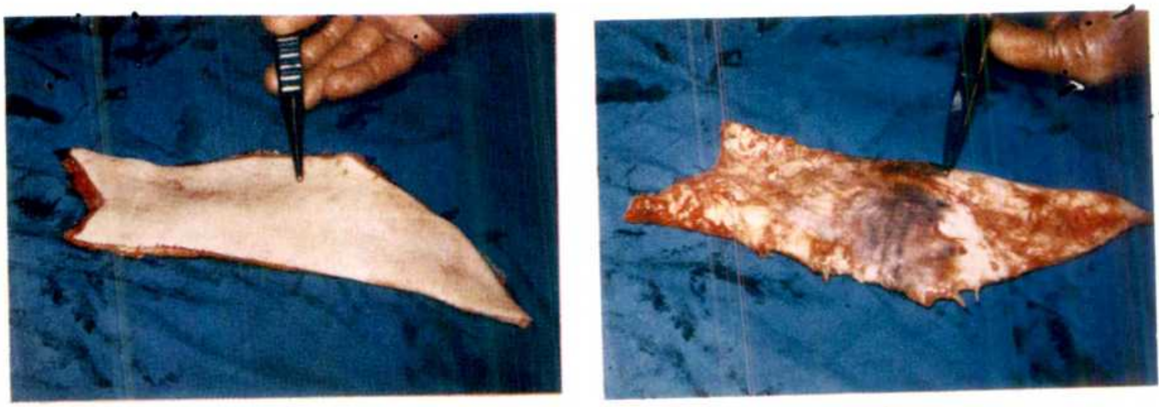
The principal clinical details are summarized in *Table I* under the headings 'Necrotizing fasciitis' and 'Progressive bacterial gangrene'.

Necrotizing fasciitis: This condition followed drainage of ischiorectal sepsis (6 patients), abdominal surgery (2 appendicectomies, 1 closure of perforated duodenal ulcer, 1 Polya gastrectomy), fracture of the pelvis (1 patient) and diabetic peripheral vascular disease (1 patient). The mean age of the patients was 49 years (range 18–73 years). Five of the patients had pre-existing systemic disease including diabetes mellitus (2 patients), actinomycosis, rheumatoid arthritis/steroid therapy and carcinomatosis.

The condition sometimes presented with non-specific redness, swelling and oedema around the primary wound or area of sepsis. In other instances the first sign was the appearance of cellulitis in an area some distance from the primarily affected region, the latter itself retaining a normal appearance. When incision was not performed at this stage the process became rapidly progressive and small areas of the skin became dusky, then blue with blister formation. Finally, overt gangrene of skin occurred, revealing in due course the characteristic grey, ragged and stringy appearance of the underlying fascia. The fascial involvement was always much more extensive than that of the related skin (*Fig.* 1). The average duration

---

* University Department of Surgery and Division of Surgery, Western Infirmary, Glasgow.



a *b*

Fig. 1. *a*, Portion of excised apparently normal skin overlying an area affected by necrotizing fasciitis. *b*, Undersurface of the same portion of skin showing the extent of fascial necrosis.

Table I: CLINICAL FEATURES OF ACUTE DERMAL GANGRENE

Case no.	Age	Sex	Site involved	Predisposing factors	Major associated factors
Necrotizing fasciitis					
1	50	M	Right flank, right lower limb	Actinomycosis in right iliac fossa, Polya gastrectomy	Septic shock, respiratory failure, disseminated intravascular coagulation, heptocellular damage
2	63	M	Right lower abdomen, upper thighs, penoscrotal	Transrectal biopsy of cancer of prostate	Toxaemia
3	54	F	Thorax, right flank, perineum	Appendicectomy (acute appendicitis)	Peritonitis, septic shock, respiratory failure
4	59	F	Anterior abdominal wall, left buttock	Left ischiorectal abscess, diabetes	Toxaemia, bronchopneumonia
5	54	M	Both flanks, perineum, scrotum, both legs, left groin	Left ischiorectal abscess, perforated sigmoid diverticulitis	Faecal peritonitis, septic shock, respiratory failure, renal failure
6	73	M	Lower abdominal wall, groin, left buttock, thigh, scrotum	Left ischiorectal abscess	Toxaemia, congestive cardiac failure
7	39	F	Left lower limb	Gangrene of left leg—below-knee amputation, diabetes	Toxaemia, dehydration, respiratory failure
8	67	F	Right flank, right iliac fossa	Perforated duodenal ulcer, closure of perforation	Toxaemia, myocardial infarction, rheumatoid arthritis, steroid therapy
9	48	M	Left thigh, left leg	Left ischiorectal abscess, carcinoma of rectum, liver secondaries	Peritonitis, septic shock, subphrenic abscess, bronchopneumonia
10	18	F	Thoraco-abdominal dorsolumbar region	Appendicectomy, acute appendicitis	Septic shock, respiratory failure, disseminated intravascular coagulation, caecal fistula
11	44	M	Anterior abdominal wall, perineum	Anal fissure, left ischiorectal abscess	Toxaemia
12	18	F	Left leg and thigh, left lower abdomen	Fractured pelvis	Toxaemia, acute pulmonary oedema, disseminated intravascular coagulation
Progressive bacterial gangrene					
1	78	M	Lower abdomen	Left orchidectomy	Toxaemia
2	70	F	Left leg	Diabetic gangrene, left below-knee amputation	Toxaemia, respiratory failure
3	77	F	Abdominal wall, upper right thigh	Diabetes, fractured neck of femur	Toxaemia, hypostatic pneumonia, pulmonary embolism, obesity
4	23	F	Right lower abdomen, right groin, perineum	Lymphopoenia, biopsy of lymph node in right groin	Toxaemia, renal failure
5	27	M	Left iliac fossa, left buttock	Road traffic accident, laceration of left buttock	Toxaemia
6	50	M	Penoscrotal region	Urethral stricture	Septic shock, respiratory failure, obesity
7	52	M	Perineum, scrotum	Left ischiorectal abscess	Toxaemia, atherosclerotic heart disease
8	38	M	Lower abdomen, left groin	Left ischiorectal abscess, diabetes	Toxaemia, relapsing pancreatitis

Table II: TREATMENT AND CLINICAL COURSE OF ACUTE DERMAL GANGRENE

Case no.	Treatment: General	Treatment: Local	Initial response to treatment	Arrest of lesion	Outcome, cause of death
Necrotizing fasciitis					
1	Antibiotics, i.v. fluids	Multiple incisions, antibiotics, OHP (3 d)	Good	No	Died (day 4). Pulmonary embolism. No post-mortem
2	Antibiotics, i.v. fluids	Multiple incisions, OHP (2 d)	Good	No	Died (day 28). Overwhelming toxaemia. No post-mortem
3	Antibiotics, i.v. fluids	Exploration of wound, OHP (3 d)	Poor	No	Died (day 16). Bronchopneumonia/peritonitis
4	Antibiotics, i.v. fluids, transverse colostomy	Multiple incisions, OHP (1 d)	Fair	No	Died (24 hours). Aspiration pneumonitis
5	Antibiotics, i.v. fluids, laparotomy, transverse colostomy	Multiple incisions, excision of necrotic fascia, OHP (8 d)	Good	Yes	Died (day 17). Renal failure, bronchopneumonia
6	Antibiotics, i.v. fluids	Multiple incisions, excision of necrotic fascia, OHP (6 d)	Good	Yes	Survived
7	Antibiotics, i.v. fluids	Desloughing, above-knee amputation, OHP (9 d)	Fair	No	Died (day 30). Overwhelming toxaemia
8	Antibiotics, i.v. fluids	Multiple incisions, OHP (4 d)	Good	No	Died (day 18). ? Pulmonary embolism. No post-mortem
9	Antibiotics, i.v. fluids, colostomy	Multiple incisions, excision of necrotic fascia and skin, OHP (2 d)	Good	Yes	Died (day 14). Bronchopneumonia
10	Antibiotics, i.v. fluids, assisted ventilation	Multiple incisions, excision of necrotic fascia and skin, multiple skin grafts	Good	Yes	Survived
11	Antibiotics, i.v. fluids, transverse colostomy	Multiple incisions, excision of necrotic fascia and skin, multiple skin grafts	Good	Yes	Survived
12	Antibiotics, i.v. fluids, transverse colostomy	Multiple incisions, excision of necrotic fascia and skin, multiple skin grafts	Good	Yes	Survived
Progressive bacterial gangrene					
1	Antibiotics, i.v. fluids, steroids	Antibiotics, OHP (7 d)	Good	Yes	Survived
2	Antibiotics, i.v. fluids	Excision of necrotic tissue, above-knee amputation, OHP (3 d)	Good	No	Died (day 22). Overwhelming toxaemia
3	Antibiotics, i.v. fluids	OHP (4 d)	Good	Yes	Died (day 11). Pulmonary embolism
4	Antibiotics, i.v. fluids	Antibiotics, OHP (7 d)	Good	Yes	Died (day 18). Massive bleeding from oropharynx
5	Antibiotics, i.v. fluids colostomy	Incision	Good	Yes	Survived
6	Antibiotics, i.v. fluids suprapubic cystostomy	Excision of necrotic tissue, skin graft	Good	Yes	Survived
7	Antibiotics, i.v. fluids	Multiple incisions, excision of necrotic tissue	Good	Yes	Survived
8	Antibiotics, i.v. fluids	Multiple incisions, excision of necrotic tissue, OHP (5 d)	Good	Yes	Survived

OHP, hyperbaric oxygen.

of time between the initiating factor and the first signs involving skin was 11 days (range 6–31 days). Coincident with the local features of progressive infection the general condition of the patient deteriorated, and toxaemia, dehydration and mental apathy rapidly ensued. In all 6 patients in whom analysis of plasma proteins was carried out hypo-albuminaemia and hypergammaglobulinaemia were found.

In 10 of the 12 patients detailed bacteriological analyses were made on specimens obtained through fresh incisions in the affected area. The commonest organisms isolated were coliforms in combination most frequently with enterococci (5) and streptococci (4); in only one case was the streptococcus of the alpha-haemolytic variety. Other associated organisms included bacteroides (3), diphtheroids (2), *Clostridium welchii* (2), proteus (2), staphylococci (1) and *Pseudomonas pyocyanea* (1). After the initial surgical incisions had been made, bacteriological cultures most regularly revealed a mixed growth of coliforms and proteus or

Ps. pyocyanea organisms, although numerous other organisms occurred as single isolates.

Because of the frequency and severity of toxaemia and dehydration, treatment aimed at improving the general condition of the patient was often as immediately important as treatment of the local infection. Thus, the administration of intravenous fluids and large doses of the appropriate systemic antibiotics was routine; penicillin or ampicillin and a broader spectrum antibiotic (usually gentamicin) formed the most frequent combination, although other antibiotics were added as indicated. Colostomy was performed in 5 patients to limit contamination of the infected area with bowel contents (and caecal fistula occurred spontaneously in a sixth).

Treatment directed at the infection itself changed during the course of the study (*Table II*). In 5 of the earlier patients (*Cases* 1, 2, 3, 4 and 8) multiple incisions were made in the affected areas and hyperbaric oxygen at 2 atm abs was administered intermittently over a period of 3 days (range 1–4 days). The response to this combined treatment was initially good in 3 patients, fair in one and poor in another. However, all 5 patients died. Death was sudden in 3 cases (on days 2, 4 and 18) with the clinical features of pulmonary embolism, and gradual in 2 with progressive toxaemia. In 6 of the later patients (*Cases* 5, 6, 9, 10, 11 and 12) radical excision of the necrotic fascia (all 6 patients) and overlying skin (4 patients) was performed; 3 had hyperbaric oxygen. Four of these 6 patients survived. In both the other patients the local necrotic process had been arrested and skin grafting was awaited. One died suddenly following perforation of a sigmoid diverticulum and the second was found at laparotomy to have secondary carcinomatosis. The remaining patient (*Case* 7) was a severe diabetic who showed little or no response to early conservative surgical management and became progressively toxic in spite of later radical surgery including above knee amputation. She died of overwhelming toxaemia on day 30 of her illness.

In 3 of the 4 patients (*Cases* 9, 10 and 12) treated by radical excision of skin overlying the involved area, the skin was preserved for later grafting. An illustrative example of one of these patients is outlined below:

Case 10: P. H., an 18-year-old woman, underwent an emergency appendicectomy for histologically proved acute appendicitis. Her postoperative recovery was complicated by continued pyrexia, vomiting and abdominal distension which was initially treated conservatively with no improvement. At re-exploration 3 days later the wound showed signs of cellulitis and it was noted that part of the external oblique aponeurosis was necrotic. A large purulent pelvic collection was encountered. The obviously necrotic portion of fascia was excised, and following evacuation of pus and irrigation of the pelvic cavity with noxytiolin a drain was inserted in the pelvic cavity and the wound closed loosely, leaving a subcutaneous drain. Culture from the pus revealed growth of lactose-fermenting coliform organisms and enterococci sensitive to gentamicin.

In spite of adequate drainage of the pelvic cavity and intravenous administration of the appropriate antibiotics and fluids, the patient remained very toxic, with a gradual fall in urine output and progressive anaemia. Because of lack of improvement, further exploration was carried out on day 11. This revealed gross undermining of the skin of a large area of the thoraco-abdominal wall and extensive necrosis of the subcutaneous tissue, although the skin itself appeared normal (*Fig.* 2). A diagnosis of necrotizing fasciitis with associated endotoxic shock was made. The skin and subcutaneous tissue of the involved part were completely excised (*Fig.* 3). Numerous bacteriological swabs were taken. The skin was defatted and preserved at 4 °C at the Regional Plastic Surgical Centre with a view to future grafting. The patient was transferred from the operating theatre to the Intensive Therapy Unit for subsequent care.

In the Intensive Therapy Unit considerable therapeutic, psychiatric and nursing problems were encountered. Frequent blood gas estimations revealed a gradual deterioration in pulmonary gas exchange necessitating the use of intermittent positive pressure ventilation via an endotracheal tube. The patient was dehydrated and acidotic and there was haematological evidence of disseminated intravascular coagulation. Bacteriological cultures from the denuded area revealed a heavy growth of coliform organisms and bacteroides. A caecal fistula developed which did not respond to simple closure.

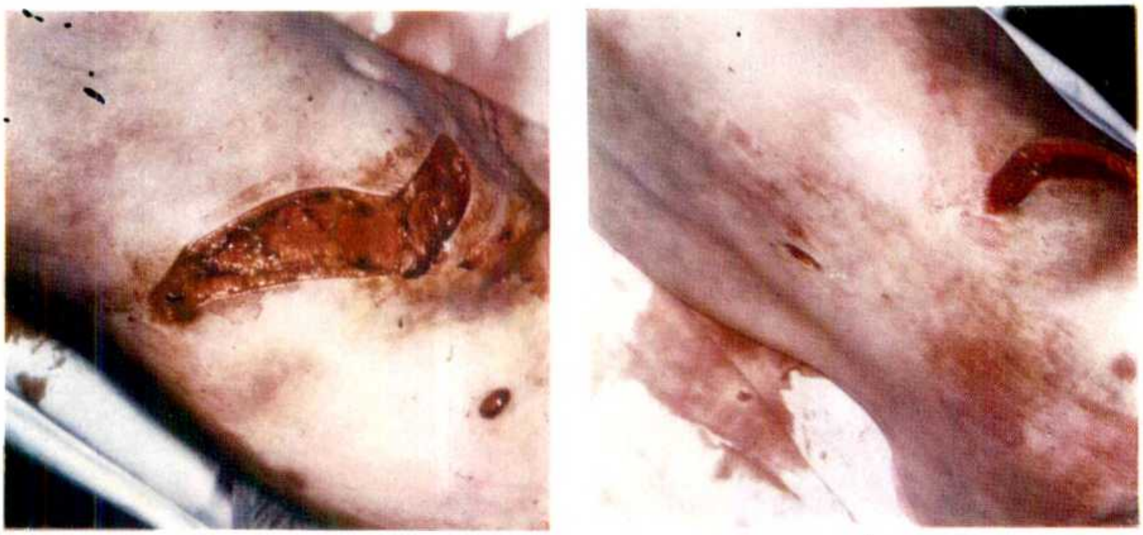
With appropriate treatment the patient gradually improved and on day 16 the endotracheal tube was removed. The initially preserved skin was applied to the denuded area but little of the graft survived. Transfer to the Regional Plastic Surgical Centre was arranged on day 20 and multiple skin grafting was performed. Complete skin cover was achieved in 3 months. The appearance of the grafted areas at 1 year is illustrated in *Fig.* 4. The caecostomy was finally closed 18 months after the original appendicectomy.

In the most recent patient (*Case* 12) the skin overlying the involved area was completely excised 5 days after the onset of the condition; 80 per cent of this skin survived after grafting 1 week later.

Progressive bacterial gangrene: This form of gangrene followed ischiorectal sepsis (3 patients), lower abdominal surgery (1 orchidectomy and 1 lymph node biopsy), urethral stricture (1 patient), fractured neck of femur (1 patient) and diabetic peripheral vascular disease (1 patient). The mean age of these patients was 52 years (range 23–78 years). Five of the patients had pre-existing systemic disease including diabetes mellitus (3 patients), persistent lymphopoenia and severe atherosclerotic heart disease.

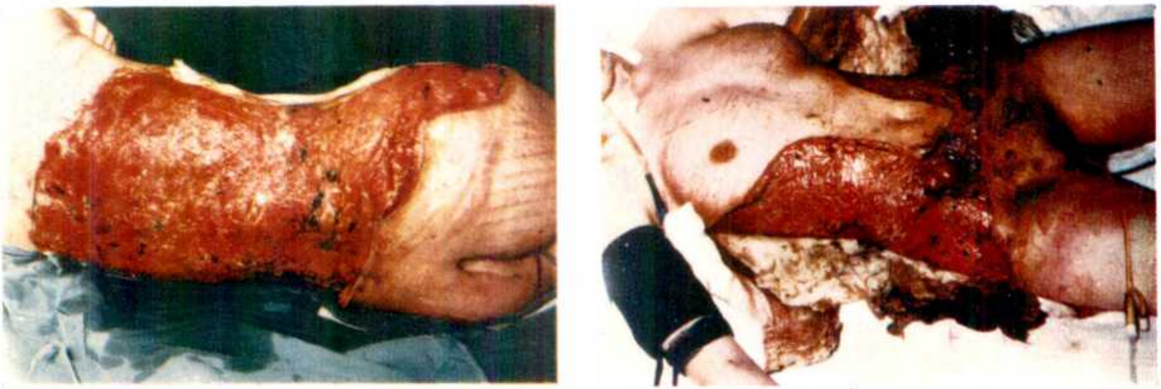
In all 8 patients bacteriological cultures were taken from fresh incisions in the affected area. The commonest organisms isolated were coliforms. Other associated organisms included bacteroides (3), *Cl. welchii* (2), haemolytic streptococci (1) and staphylococci (1). The most frequent colonizing organisms were coliforms (4) associated with proteus in 2 patients and *Ps. pyocyanea* and *Staphylococcus aureus* in 1 patient each. In one of the patients (*Case* 1) bacteriological cultures were consistently negative.

The condition usually presented with a non-specific cellulitis around the wound or near the site of sepsis. The abdominal wall lesions soon developed a characteristic appearance with a central necrotic zone, an advancing, often serpiginous, purplish zone and a peripheral erythematous margin fading gradually towards normal skin. In the case of penoscrotal lesions skin gangrene was rapidly progressive and the purplish marginal zone was not obvious. Irrespective of site, the whole skin thickness was primarily involved and there was little or no invasion of subcutaneous tissues. Unlike necrotizing fasciitis this form of acute dermal gangrene followed the initiating factor without an



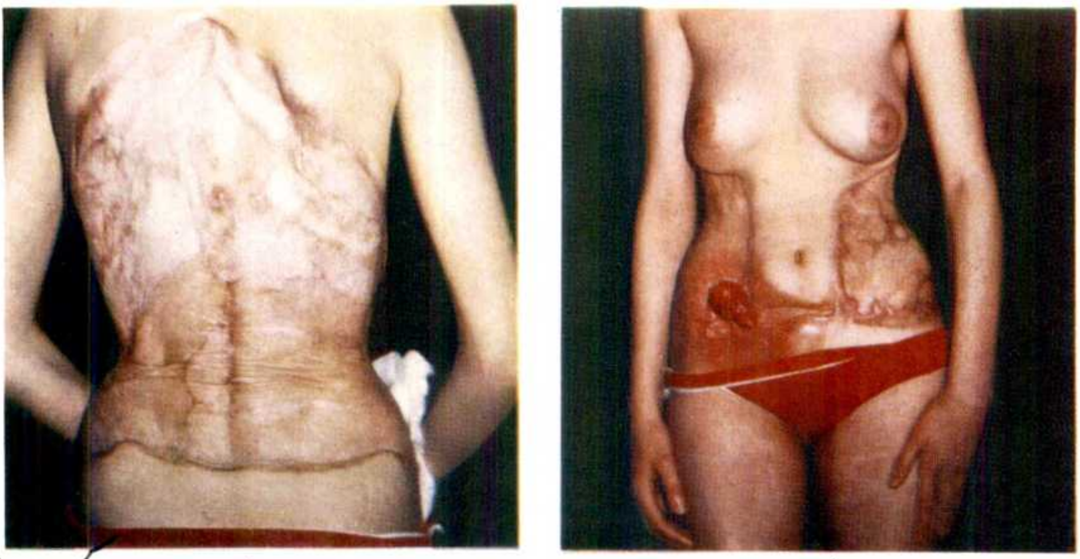
a *b*

Fig. 2. *Case* 10. Relatively normal appearance of abdominal (*a*) and dorsolumbar (*b*) skin on day 11 when radical excision was performed.



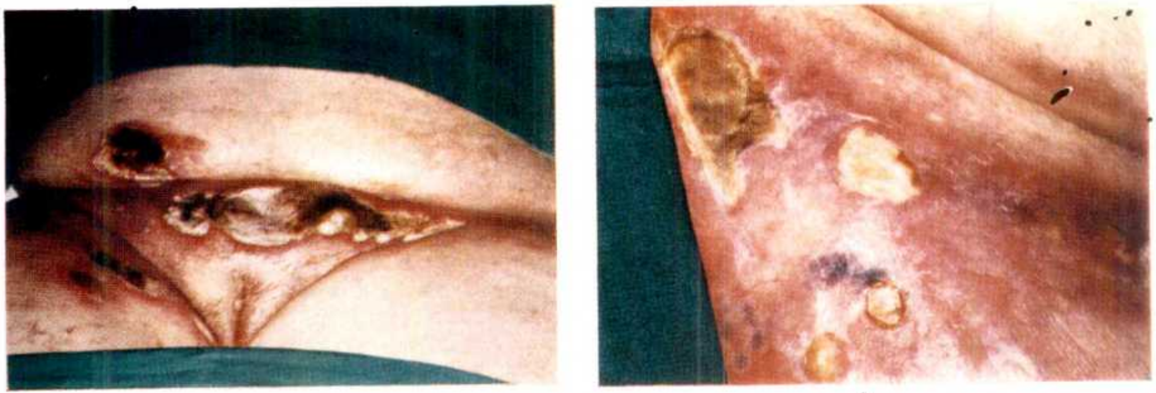
a *b*

Fig. 3. *Case* 10. Posterior (*a*) and anterolateral (*b*) extent of excision of skin and necrotic fascia.



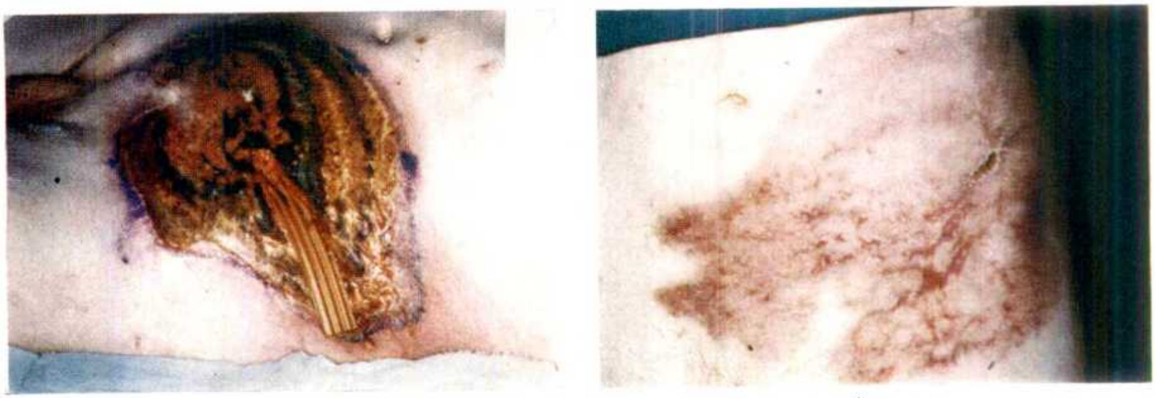
a *b*

Fig. 4. *Case* 10. Appearance of the grafted posterior (*a*) and anterolateral (*b*) area at 1 year.



a *b*

Fig. 5. *Case* 3. *a*, Lower abdominal wall and pubis showing a gangrenous lesion. *b*, Distant lesions affecting the upper right thigh showing characteristic purplish advancing margins.



a *b*

Fig. 6. *Case* 1. *a*, Extensive area of the left abdominal wall involved in a progressive gangrenous lesion. *b*, Spontaneous epithelization several weeks later.

apparent quiescent interval. The patient's general condition deteriorated with spread of the local infection but rarely to the same degree of severity as in the patients with necrotizing fasciitis. Hypo-albuminaemia and hypergammaglobulinaemia were marked in 3 of the 4 patients in whom analysis of plasma proteins was performed.

Treatment of the patient's general condition was of major importance and consisted of the administration of intravenous fluids and antibiotics; colostomy and suprapubic cystostomy were performed in 2 of the patients.

In 6 of the patients (*Cases* 2, 3, 5, 6, 7 and 8) it was obvious from the outset that all the layers of the skin were involved, and in these, local treatment consisted of either incision or early excision of necrotic tissue. Three of the most severely ill of these patients received hyperbaric oxygen. The initial response to the combination of treatment was good in all 6 patients although in 1 patient the lesion was not finally arrested. Four survived with complete healing of the skin lesions One patient died suddenly on day 11 from pulmonary embolism, and the other, an elderly diabetic, succumbed to progressive overwhelming toxaemia on day 22.

In 2 of the patients (*Cases* 1 and 4) the condition seemed to be limited clinically to the epidermal layers of skin, and in these, local treatment consisted of non-adherent dressings and hyperbaric oxygen. In both patients the initial response to treatment was good and the local condition was arrested. The younger patient died suddenly on day 18 after massive oropharyngeal bleeding, probably aggravated by severe thrombocytopenia. The older patient survived with spontaneous healing of the affected area.

Illustrative examples of 2 of the patients in this group are outlined below.

Case 3: G. H., a 78-year-old woman, was admitted to another hospital with a fracture of the neck of the right femur. At the time of admission the patient was noted to have a small patch of gangrenous skin in the suprapubic region which spread rapidly during the course of the next 2 days with surrounding inflammatory oedema and surgical emphysema. Bacteriological studies revealed heavy growth of coliform and bacteroides organisms.

In spite of the administration of appropriate antibiotics, her condition deteriorated. She became toxic and a rapidly spreading cellulitis was noted. Further bacteriological studies revealed a heavy growth of bacteroides, anaerobic streptococci and proteus organisms. At this stage diabetes mellitus was discovered for the first time and treatment with soluble insulin was started. Transfer to the Hyperbaric Unit was arranged on the eighth day by which time there was an extensive area of necrosis of the lower abdominal wall and upper right thigh (*Fig.* 5). Hyperbaric oxygen therapy was started at 2·5 atm abs in sessions not exceeding 2½ hours continuously. The patient's condition improved and 48 hours after hyperbaric oxygen therapy it was considered that the progress of the infection had been halted. Over the next 24 hours, however, the improvement was not sustained and the patient died suddenly on the eleventh day. A post-mortem examination revealed organizing ante-mortem thrombi in the pulmonary arteries.

Case 1: W. W., a 78-year-old man, underwent a left orchidectomy through an inguinal incision for a benign testicular mass. Six days later an ischaemic lesion appeared in the wound. In spite of local treatment the lesion extended over the lower abdomen during the next few days, and at the time of admission to the Western Infirmary (day 22) the greater part of the left lower quadrant of the abdomen was involved (*Fig.* 6*a*). An incision into the affected area suggested that the deeper layers of the skin and subcutaneous tissues were not involved in the process, but histological examination of biopsy material indicated some spread to deeper layers.

The initial bacteriological studies failed to reveal any growth, an observation which was confirmed on ten subsequent wound cultures. The patient was subjected to an intensive course of hyperbaric oxygen over the next week. In addition, parenteral and local antibiotics were administered in spite of the negative bacteriological reports. The patient's progress following this combined therapy was satisfactory and gradual spontaneous epithelization occurred over the subsequent weeks (*Fig.* 6*b*).

Discussion

The clinical conditions described in this study readily fell into two categories: one in which skin gangrene succeeded a major infective process in the subcutaneous tissues, and the other in which skin gangrene related directly to infection of the skin.

Necrotizing fasciitis

The first of these two clinical conditions was described many years ago (Meleney, 1924), but the term 'necrotizing fasciitis' was not used until relatively recently (Wilson, 1952). The term is appropriate since the primary condition is a progressive necrosis of the superficial fascia, subcutaneous fat and superior surface of the deep fascia with death of skin secondary to thrombosis of the subcutaneous blood vessels. Tissues deep to the fascia are not normally involved.

The diagnosis of necrotizing fasciitis is not difficult to establish once the characteristic necrotic appearance of the fascia is visualized, but in the early stages the relatively normal appearance of the skin conceals the severity and extent of the underlying disease. The diagnosis can only be confirmed with certainty by immediate exploratory incisions. The condition is readily distinguished from 'gas gangrene' which normally occurs in association with penetrating wounds following major trauma and involves, in its florid form, invasion of muscle by clostridia organisms. Crepitus and a 'mousy' smelling discharge are characteristic. The patient becomes rapidly toxic and is often restless and delirious.

Although the original description of necrotizing fasciitis has survived the passage of time some of the features of the condition appear to have changed. In some, predominantly early, reports (Meleney, 1924, 1933; Wilson, 1952; Strasberg and Silver, 1968) the disease commonly occurred in the extremities, often after minor trauma, whereas in several recent publications (Rea and Wyrick, 1970; Wilson and Haltalin, 1973) the trunk, and in particular the lower abdomen, was the most commonly affected site. The bacteriological pattern appears also to have undergone a change with the passage of time. In Meleney's (1924) series haemolytic streptococci were exclusively isolated, but later the bacterial flora included haemolytic staphylococci (Wilson, 1952) and various Gram-negative organisms (Crosthwait et al., 1964; Meade and Mueller, 1968; Rea and Wyrick, 1970). In the present series the bacteriological cultures taken directly from the necrotic fascia through freshly incised wounds revealed a wide variety of organisms. In all but one case haemolytic streptococci were absent. Two factors may have prevented the demonstration of these organisms on bacteriological culture: the early use of antibiotics, including topical applications, prior to consideration of the diagnosis of necrotizing fasciitis, and rapid overgrowth with essentially faecal organisms in wounds predominantly of the lower abdomen and perineum. Nevertheless, it is surprising that only one isolate of haemolytic streptococci was made, and it is possible that while these organisms may be important in initiating the disease process, their presence may not be critical for its subsequent progression.

The effect of treatment also appears to have changed over the years. In early reports, incision of the affected area together with frequent antiseptic soaks and careful débridement of necrotic tissue was attended by excellent results, with the reported mortality as low as 9 per cent (Wilson, 1952). Nowadays such relatively conservative procedures appear less effective unless used at a very early stage, and mortality in some series ranges between 30 and 40 per cent (Crosthwait et al., 1964; Rea and Wyrick, 1970; Wilson and Haltalin, 1973). It is possible that only the most resistant infections are now reported and that infections involving the extremities in young, otherwise healthy individuals respond rapidly to incision, débridement and antibiotics. Infections of the trunk and perineum are more difficult to drain adequately and diagnostic incisions may be delayed in the elderly or very sick patient. On the basis of present experience the best results appear to follow early, multiple and extensive incisions into the affected area with complete excision of the underlying necrotic fascia. Whether the large flaps of skin thus created should simply be reflected or excised and stored is debatable, but if there is any doubt about the adequacy of drainage the latter alternative is preferable and is best done at one operation. This policy was adopted in 4 of the most recent patients and the excised skin later regrafted in 2.

The role of hyperbaric oxygen in the treatment of this condition is uncertain. The patient's general condition normally improved after hyperbaric oxygen but the latter was usually only one of the therapeutic changes introduced on initial referral. Other factors, e.g. alterations in the antibiotic regimen or in intravenous fluid administration, may have played an equally important role. Certainly hyperbaric oxygen did not halt spread of the necrotic process in patients whose skin flaps were not reflected. This pattern of response to hyperbaric oxygen was readily distinguishable from that in most patients with 'gas gangrene' treated at this centre in whom hyperbaric oxygen combined with simple incision is usually associated with rapid cessation of the primary condition. The patient with the most extensive involvement (*Case* 10) survived because of the radical nature of the surgical procedure; she did not have hyperbaric oxygen treatment. Present experience would suggest, therefore, that surgical treatment is of prime importance. Whether hyperbaric oxygen adds anything to surgical management remains to be determined. Antibiotics were usually administered early in the course of the illness and appear to have been the appropriate choice in most cases. Like hyperbaric oxygen, however, the role of antibiotics seems to be secondary to radical surgical treatment.

Progressive bacterial gangrene

The conditions included under this heading have in the past been considered as separate clinical entities. For example, 'postoperative progressive synergistic gangrene' was so called because lesions answering the clinical description of 4 of the patients in the present series (*Cases* 1, 3, 4 and 5) appeared to be caused by a pair of organisms which were more active in combination than alone. Originally the pair most frequently incriminated were a non-haemolytic microaerophilic streptococcus and *Staph. aureus* (Meleney, 1933), but subsequently several synergistic pairs have been demonstrated, including proteus and *Staph. albus* (Lyall and Stuart, 1948) and coliforms and *Ps. aeruginosa* (Webb and Berg, 1966). 'Fournier's gangrene' was the original name attached to lesions similar to those described in 3 of the patients of the present series (*Cases* 6, 7 and 8). These gangrenous lesions of the scrotum and penis were considered to be due to invasion by haemolytic streptococcus (Meleney, 1933). 'Synergistic necrotizing cellulitis' might well have been the name applied to the final patient of this series (*Case* 2), in whom widespread invasion of an amputation stump was attributed to a synergistic combination of aerobic Gram-negative rods and an anaerobic streptococcus, with bacteroides as a frequently associated organism (Stone and Martin, 1972).

Recently, the justification for these separate subgroups has been questioned since they are almost certainly at most variants of a single process (Pillsbury et al., 1956; Rook et al., 1972).

Examination of the bacteriological pattern reported in the present study does not support the concept that one specific combination of organisms underlies this condition. In only one of the patients, with scrotal gangrene, did culture reveal haemolytic streptococci; the majority of the remainder of the series had a mixture of coliform organisms with one of the bacteroides or clostridial family—not an unexpected combination in wounds of the lower abdomen and perineum. Synergism between some of these groups may exist but presumably not more so than in many other wounds similarly infected.

Although there may have been historically valid reasons for separating the subgroups on the grounds of differing therapy, this does not now seem to be necessary. Whereas the earlier literature suggested the need for wide and radical excision of the affected area in the case of so-called 'progressive synergistic gangrene', in recent years simple incision and drainage combined with appropriate antibiotics in adequate doses seem to suffice. The use of hyperbaric oxygen in 5 of the 8 patients in the present series appeared to contribute to the arrest of the lesion in all but one. Apparent disappearance of the anaerobic organisms from the wounds may, in part, explain the role of hyperbaric oxygen in this condition.

General comments

Both these forms of acute dermal gangrene are relatively rare in modern surgical practice. The advent of antibiotics has presumably helped to reduce the incidence of the condition and there seems little doubt that the cases reported in the current literature represent a group in which infection is only one of the factors involved. Ischaemia and reduced host defence mechanism may be equally important factors.

In necrotizing fasciitis the relative avascularity of the fascial planes may favour the subcutaneous spread of infection, particularly with anaerobic organisms. A number of the patients had underlying systemic illness to which was added hypoproteinaemia and presumably other deficiencies as the illness progressed. The patient's ability to resist sustained infection was thus substantially reduced. In progressive bacterial gangrene avascularity of the wound and reduced host defence mechanisms appear to have contributed to the progress of the lesion in some instances, although specific immunological defects were not adequately investigated.

Thus, while earlier reports describing acute dermal gangrene stressed the importance and apparent specificity of the invading organisms, it now seems clear that the main problems confronting the surgeon is a vicious cycle of infection, local ischaemia and reduced host defence mechanisms. Which of these factors predominates in the inidividual patient will vary, but it is vital that all three are considered simultaneously if arrest of the progress of these lesions is to be achieved and lives saved.

Acknowledgements

We gratefully acknowledge the collaboration of the many colleagues, both at the Western Infirmary, Glasgow, and elsewhere in the United Kingdom, who have referred patients to us. We are also grateful to Dr J. D. Sleigh, Consultant Bacteriologist, Western Infirmary, Glasgow, who read and criticized the bacteriological component of the paper.

References

CROSTHWAIT R. W. jun., CROSTHWAIT R. W. and JORDAN G. L. jun. (1964) Necrotizing fasciitis. *J. Trauma* 4, 148–157.

LYALL A. and STUART R. D. (1948) Progessive post-operative gangrene of the skin. Observations on aetiology and treatment in two cases. *Glasg. Med. J.* **29**, 1–18.

MEADE J. W. and MUELLER C. B. (1968) Necrotizing infections of subcutaneous tissues and fascia. *Ann. Surg.* **168**, 274–280.

MELENEY F. L. (1924) Haemolytic streptococcus gangrene. *Arch. Surg.* **9**, 317–364.

MELENEY F. L. (1933) A differential diagnosis between certain types of infectious gangrene of the skin. *Surg. Gynecol. Obstet.* **56**, 847–867.

PILLSBURY D. M., SHELLEY W. B. and KLIGMAN A. M. (1956) *Dermatology.* Philadelphia, Saunders, pp. 492–496.

REA W. J. and WYRICK W. J. jun. (1970) Necrotizing fasciitis. *Ann. Surg.* **172**, 957–964.

ROOK A., WILKINSON D. S. and EBLING F. J. G. (1972) *Textbook of Dermatology.* Oxford, Blackwell, p. 498.

STONE H. H. and MARTIN J. D. jun. (1972) Synergistic necrotizing cellulitis. *Ann. Surg.* **175**, 702–710.

STRASBERG S. M. and SILVER M. S. (1968) Haemolytic streptococcus gangrene. **115**, 763–768.

WEBB R. and BERG E. (1966) Symbiotic gangrene due to *Pseudomonas pyocyanea* and *E. coli. Aust. NZ J. Surg.* **36**, 159–160.

WILSON B. (1952) Necrotizing fasciitis. *Am. Surg.* **18**, 416–431.

WILSON H. D. and HALTALIN K. (1973) Acute necrotizing fasciitis in childhood. *Am. J. Dis. Child.* **125**, 591–595.

Br. J. Surg. Vol. 62 (1975) 373-374

Gas gangrene of the extremity: the presenting clinical picture in perforating carcinoma of the caecum

R. MZABI, H. S. HIMAL AND L. D. MacLEAN*

SUMMARY

This paper reports 2 diabetic patients with perforating carcinoma of the caecum and gas gangrene of the pelvis and right lower extremity in whom the infective process was the main clinical feature.

ACCORDING to Goligher and Smiddy (1957), 7 per cent of all cases of carcinoma of the large intestine present with perforation of the bowel and either localized or generalized peritonitis. Perforation within the tumour itself leading to localized peritonitis and abscess formation is more characteristic of caecal lesions (Ewing, 1951; Patterson, 1956).

A recognized complication of carcinoma is gas gangrene (Cabrera et al., 1965), with a very high associated mortality.

Case reports

Case 1: Mrs C. J., a 71-year-old diabetic female treated with parenteral insulin, was admitted to the Royal Victoria Hospital, Montreal, with the diagnosis of acute gangrene of the right lower extremity due to atherosclerotic vascular disease. She had not been feeling well for about 1 month and on the night prior to admission had had several episodes of nausea and vomiting. On the morning of the day of admission the patient had noted pain in the right leg and foot. The pain had intensified and the patient was brought to hospital. Clinical examination revealed a pale sweating female complaining of severe pain in the right lower extremity. The blood pressure was 140/80, the pulse was 100/min and regular and the oral temperature was 38 °C. The abdomen was tense with minimal guarding and no tenderness. Re-examination of the abdomen with minimal analgesia revealed no abnormality.

The right lower extremity was cold and pale and crepitations extended from the foot to the thigh. Only the right femoral pulse was present and was normal to palpation. Urinalysis revealed 2+ glucose and there was a marked leukocytosis (25 600 ml/mm).

With the diagnosis of gas gangrene of the right lower extremity, chloromycetin 500 mg intravenously was given and the patient was taken to the operating theatre where a right supracondylar amputation was performed. During the procedure gas was noted to be present in the fascial planes. At the conclusion of the operation the patient became hypotensive and cardiac arrest ensued. Resuscitation was unsuccessful, and the patient died 4 hours after admission to hospital.

Post-mortem examination revealed a large fungating anaplastic carcinoma of the caecum which had perforated. The anterior caecal wall was gangrenous with fibropurulent peritonitis in the vicinity. *Clostridium septicum* was cultured from the wall of the caecum as well as from the stump of the right thigh. Gas gangrene was present in the muscles of the right pelvis, right thigh stump and anterior abdominal wall.

Case 2: Mrs B. F., a 78-year-old diabetic female, was admitted complaining of pain in the right hip. There was no antecedent trauma. Several years prior to admission the right fifth toe had been amputated for gangrene.

The blood pressure was 190/90, the pulse was 85/min and the oral temperature was 38·4 °C. The abdomen was soft and non-tender. The right hip was painful to movement. Urinalysis revealed 3+ glucose. Random blood sugar was 420 mg per cent. An X-ray revealed a non-displaced fracture involving the greater trochanter. The presence of gas was noted in the soft tissues of the right pelvis, hip and thigh.

Later that evening the abdomen became distended and vomiting occurred. Clinical subcutaneous emphysema appeared along the right thigh and buttock. Hypotension also developed. A diagnosis of perforated viscus was made and the patient was taken to the operating theatre. However, she died before laparotomy could be performed.

Post-mortem analysis revealed a fungating well-differentiated adenocarcinoma of the posterior wall of the caecum which had perforated. Fibrinous adhesions were present between the tumour and the right iliopsoas muscle. The right thigh muscles, including the iliopsoas muscle, were necrotic. *Clostridium tertium*, anaerobic streptococci and *Escherichia coli* were cultured from the right iliopsoas and right thigh muscles.

Discussion

Caecal carcinoma commonly presents as a triad—abdominal mass, anaemia and weight loss. Rarely, these tumours present with perforation (Ransom, 1939; Brown et al., 1948).

Gas gangrene of the extremities as the presenting initial clinical picture is exceptional. Kimball and Rawson (1952) described a patient who presented with gas gangrene of the left arm. She died prior to initiation of therapy; autopsy revealed adenocarcinoma of the caecum with retroperitoneal perforation and necrosis and crepitations of the retroperitoneal tissues. Gazzaniga (1967) reported an 81-year-old diabetic woman who presented with crepitation and pain in the right upper extremity. She was taken to the operating theatre where right arm disarticulation was performed. However, the patient died several hours later. Post-mortem examination revealed generalized haemolysis, endocarditis and myocarditis and a large and extensive adenocarcinoma of the caecum with focal ulceration, but without any evidence of perforation. Cultures from the arm grew *Clostridium welchii*. The cause of death was clostridial septicaemia.

Valentine (1957) reported a 70-year-old man who presented with pain in the left hip after a fall. He had previously been admitted to hospital because of abdominal pain with a mass in the right iliac fossa. An appendiceal abscess was diagnosed; the patient was treated conservatively and sent home with the view to interval appendectomy. Several hours after his second admission there was crepitus and bruising of the left hip. Two hours later he died. Post-mortem examination revealed necrosis and haemorrhage into the muscles of the left thigh. An ulcerating carcinoma of the caecum was also present. *C. septicum* was cultured from the necrotic muscles. Camblin and Kinley (1970) reported a 74-year-old man who presented with severe pain in the left thigh. Physical examination revealed generalized tenderness over the abdomen, maximal at the right iliac fossa. The left thigh was swollen, bruised, tender and crepitant. Laparotomy revealed a large fungating carcinoma of the caecum without evidence of perforation. A right hemicolectomy and excision of necrotic tissue in the left thigh were carried out. However, the patient died several hours later. *C. septicum* was cultured from the left thigh.

---

* Department of Surgery, Royal Victoria Hospital and McGill University, Montreal, Canada.

Requests for reprints to Dr H. S. Himal, Department of Surgery, Royal Victoria Hospital, 687 Pine Avenue West, Montreal, Canada H3A 1A1.

In the 4 patients described above, although cultures of the necrotic areas revealed clostridial organisms, bacteriological studies on the caecal carcinomas were not performed. Septicaemia occurred with colonization of muscles of the extremities leading to myonecrosis.

Clostridia are normal inhabitants of the digestive tract and can be easily isolated and cultured from the faeces (MacLennan, 1962). Tissue necrosis is a necessary antecedent to clostridial myositis. In the 2 case reports presented here, necrotizing carcinoma of the caecum with local infection caused an environment conducive to spread of the organisms along the retroperitoneal tissue planes including the iliopsoas muscle. The necrotizing myositis soon spread to the lower extremity which then became the main clinical problem. Similar patterns of spread have been reported complicating appendicitis (Gordon, 1936), diverticulitis (Dawson and Hardy, 1948; Nichols 1961) and carcinoma of the left colon and rectum (Wyman, 1949; Whyland and Levin, 1960). *Clostridium perfringens*, *C. septicum*, *C. novyi*, *C. histolyticum*, *C. fallax* and *C. bifermentans* under the appropriate conditions will cause tissue necrosis and myositis (MacLennan, 1962). *C. tertium*, on the other hand, does not cause gas gangrene (MacLennan, 1962), but this organism in conjunction with anaerobic streptococci and *E. coli* can lead to necrosis, as demonstrated in one of our patients.

The presence of diabetes mellitus in both patients may have played an important role in the development of tissue necrosis. Both clostridial and non-clostridial gas gangrene is more common in diabetic patients (Wills and Reece, 1960; Brightmore, 1971; Weinstein and Barza, 1973).

The main aspect in the management of these patients is an early awareness of the underlying cause. Early diagnosis and surgery of the caecal carcinoma are of prime importance. Abdominal X-rays demonstrating gas within the tissues strongly suggest gas gangrene. In patients with perforating carcinoma of the caecum and associated myonecrosis, treatment must consist of early intensive fluid management prior to the development of toxaemia and shock. Surgical therapy must include excision of the carcinoma, extensive débridement of all necrotic tissue and adequate antibiotic cover.

References

BRIGHTMORE T. (1971) Non-clostridial gas infection. *Proc. R. Soc. Med.* **64**, 1084–1085.

BROWN C. H., COLVERT J. R. and BRUSH B. E. (1948) Clinical aspects of carcinoma of the cecum and ascending colon: report of 60 cases. *Ann. Intern. Med.* **28**, 940–948.

CABRERA A., TSUKADA Y. and PICKREN J. W. (1965) Clostridial gas gangrene and septicemia in malignant disease. *Cancer* **18**, 800–806.

CAMBLIN J. G. and KINLEY J. G. (1970) Non-traumatic clostridial myonecrosis. *Ulster Med. J.* **39**, 150–153.

DAWSON R. L. G. and HARDY R. H. (1948) Diverticulitis presenting as emphysematous cellulitis of leg—clinical report on two cases. *Br. Med. J.* **1**, 498–499.

EWING M. R. (1951) Inflammatory complications of cancer of the caecum and ascending colon. *Postgrad. Med. J.* **27**, 515–522.

GAZZANIGA A. B. (1967) Non-traumatic clostridial gas gangrene of the right arm and adenocarcinoma of the cecum: report of a case. *Dis. Colon Rectum* **10**, 298–300.

GOLIGHER J. C. and SMIDDY F. G. (1957) The treatment of acute obstruction or perforation with carcinoma of the colon and rectum. *Br. J. Surg.* **45**, 270–274.

GORDON S. (1936) *B. welchii* infection complicating conservatively treated appendiceal abscess. *Br. J. Surg.* **24**, 399–401.

KIMBALL H. W. and RAWSON A. J. (1952) Non-traumatic gas gangrene. *Va Med. Mon.* **79**, 269–271.

MACLENNAN J. D. (1962) The histotoxic clostridial infections of man. *Bact. Rev.* **26**, 177–276.

NICHOLS J. B. (1961) A case of massive gas gangrene. *Br. Med. J.* **2**, 940.

PATTERSON H. A. (1956) The management of cecal cancer discovered unexpectedly at operation for acute appendicitis. *Ann. Surg.* **143**, 670–681.

RANSOM H. K. (1939) Carcinoma of the right colon. *Surgery* **5**, 340–357.

VALENTINE J. C. (1957) Gas gangrene septicaemia due to carcinoma of the caecum and muscular trauma. *Br. J. Surg.* **44**, 630–632.

WEINSTEIN L. and BARZA M. A. (1973) Gas gangrene—current concepts. *New Engl. J. Med.* **289**, 1129–1131.

WHYLAND W. A. and LEVIN M. N. (1960) Gas gangrene without visible portal of entry. *Am. J. Surg.* **99**, 77–79.

WILLS M. R. and REECE M. W. (1960) Non-clostridial gas infections in diabetes mellitus. *Br. Med. J.* **2**, 566–568.

WYMAN A. L. (1949) Endogenous gas gangrene complicating carcinoma of colon. *Br. Med. J.* **1**, 266–267.

Br. J. Surg. Vol. 62 (1975) 375–378

Wound infections due to *Bacteroides fragilis* following intestinal surgery

D. A. LEIGH*

SUMMARY

Ninety-six wound infections due to Bacteroides fragilis occurring after intestinal surgery are described. Most infections followed appendicectomy or colectomy for diverticulitis.

B. fragilis was isolated in pure growth from 47 per cent of infections, and in mixed culture the other common bacteria were Klebsiella spp., Escherichia coli and Enterobacter spp.

Fifty-three per cent of the infections responded rapidly to either non-specific measures or antibiotic therapy, but 47 per cent of patients developed complications, usually abscess formation.

The successful isolation of bacteroides from clinical material requires special precautions. The specimen for bacteriological examination must be sent to the laboratory in a transport medium which maintains an anaerobic environment and the culture techniques must include a selective agar for the isolation of anaerobic bacteria.

The role of antibiotic therapy in preventing postoperative wound infection after intestinal surgery is discussed. Bacteroides has an unusual pattern of antibiotic susceptibility and it is essential that an effective antibiotic such as lincomycin is included in the treatment of infection originating from the intestinal tract.

THERE has recently been revived interest in the importance of anaerobic bacteria and their role in postoperative infection, particularly following gastro-intestinal surgery. Anaerobic bacteria are the predominant group of organisms in the faeces and account for over 90 per cent of the total bacterial population. These bacteria are highly sensitive to aerobic conditions and changes in temperature and are difficult to isolate routinely in the laboratory unless special culture techniques are used. *Bacteroides fragilis* is the species most frequently isolated but its incidence in wound infections following intestinal surgery is not known. After appendicectomy 93 per cent of wound infections were due to bacteroides (Leigh, 1974a), and in patients with anaerobic bacteriaemia 73 per cent had underlying gastrointestinal disease (Wilson et al., 1972). Gillespie and Guy (1956) and Gunn (1956) reported that the majority of bacteroides infections followed intestinal surgery.

The successful isolation of anaerobic bacteria from surgical infections requires careful collection of the specimen and protection in a transport medium which maintains an anaerobic environment during transit to the laboratory.

This paper presents the details of a group of 96 patients who developed wound infection due to *B. fragilis* following intestinal surgery, describes the measures necessary for successful isolation and discusses the role of antibiotic therapy.

Patients and collection of specimens

All the patients included in the study were admitted for emergency or elective surgery to the intestinal tract and had developed severe wound infections which were associated with fever, pain and a purulent discharge. Swabs were taken from the wound infection and were sent to the laboratory in either Stuart's transport medium or Robertson's meat broth. Specimens of pus or purulent fluid were also collected at the time of the operation from patients with obvious intra-abdominal infection. Patients with formed abscesses at the time of surgery were excluded. Details of antibiotic therapy and the postoperative progress of the patients were obtained either from the Control of Infection records or the inpatients' notes. All wound infections were inspected by the Control of Infection sister.

The outcome of the infection was considered successful when there was a rapid response to either antibiotic therapy or non-specific therapeutic measures. Complications were present when an abscess developed from the initial infection or the infection persisted despite appropriate therapy.

Laboratory techniques

The specimens were examined as soon as possible after arrival in the laboratory. All the swabs were cultured on to simple blood agar, MacConkey's agar, a selective blood agar plate containing 0·01 per cent neomycin, haemin 5 μg/ml and vitamin K 0·2 μg/ml and into Robertson's meat broth. The plates were incubated aerobically and anaerobically using the Gaspak (BBL, Maryland) method and examined at 24 and 48 hours. Subculture from the Robertson's meat broths was carried out on to a similar set of agar plates. The strains of *B. fragilis* were identified by routine bacteriological methods (Cowan and Steel, 1965), and antibiotic sensitivity tests were carried out by the impregnated disc technique.

Results

The primary site of surgery and probable source of the 96 *B. fragilis* infections is shown in *Table I.* Sixty-one of the wound infections were associated with appendicectomy, and in 37 perforation of the appendix had occurred. Four infections followed an elective appendicectomy carried out in association with other surgical procedures. There were 4 infections following

---

* Wycombe and Amersham General Hospitals, High Wycombe, Buckinghamshire.

surgery to the ileum, 3 of which were in patients with Crohn's disease. Thirty-one infections followed operations on the large intestine; 16 in patients with diverticulitis including 6 where perforation of a diverticulum had occurred, and 12 where carcinoma was found.

Table I: SOURCE OF INFECTION IN 96 PATIENTS

Site of surgery	Disease	No. of cases	
Appendix	Acute appendicitis	20	61
	Perforated appendicitis	37	
	Routine appendicectomy	4	
Ileum	Ischaemia	1	4
	Crohn's disease	3	
Colon and rectum	Ischaemia	3	31
	Diverticulitis	10	
	Perforated diverticulitis	6	
	Carcinoma		
	Caecum	1	
	Colon	8	
	Rectum	3	

Table II: ASSOCIATED BACTERIA IN 52 WOUND INFECTIONS WITH MIXED CULTURES

Bacteria		No.	%
Gram negative:	*Klebsiella* spp.	21	40
	Escherichia coli	14	27
	Enterobacter spp.	13	25
	Proteus spp.	4	8
	Pseudomonas aeruginosa	3	6
Gram positive:	Anaerobic streptococci	4	8
	Streptococcus faecalis	3	6
	β-Haemolytic streptococci	1	
	Clostridium welchii	1	
	Staphylococcus albus	1	

Table III: INCIDENCE OF COMPLICATIONS

Disease	Incidence of complications (%)	Nature of complication
Acute appendicitis	45	Abscess: wound 7, pelvic 1, appendix 1
Perforated appendicitis	46	Abscess: wound 13, subphrenic 2, pelvic 1, abdominal wall 1
Routine appendicectomy	50	Abscess: wound 1, abdominal wall 1
Ileum	33	Abscess: generalized abdominal 1
Diverticulitis	70	Abscess: wound 3, pelvic 1, persisting sinus 3
Perforated diverticulitis	50	Abscess: pelvic 2 (death 1)
Carcinoma	50	Abscess: wound 5, generalized abdominal 1

Table IV: ISOLATION RATE OF BACTEROIDES IN MAJOR INTESTINAL SURGERY

Year	Total no. of operations	Wound infections		Bacteroides isolated	
		No.	%	No.	%
1970	1200*	123	10	16	13
1971	1272	145	11	20	14
1972	1380	155	11	35	22
1973	1328	200	15	120	60

* Approximate total

In 26 (27 per cent) of the 96 patients who developed wound infection, swabs taken at the time of surgery grew the bacteria later responsible for the wound infection.

B. fragilis was isolated in pure growth from 44 (47 per cent) of the infections. Where a mixed growth was present (*Table II*) the commonest associated organism was *Klebsiella* spp. (40 per cent). A pure growth was found more frequently where carcinoma was present (83 per cent), and less commonly where perforation of the appendix (29 per cent) or large bowel (40 per cent) had occurred.

Fifty-one (53 per cent) of the wound infections responded rapidly either without specific therapy or with antibiotic therapy. Forty-five (47 per cent) patients developed complications, usually wound abscess or metastatic abscesses such as subphrenic or pelvic, and 1 patient died of the infection. The incidence of complications was highest (70 per cent) in diverticulitis (*Table III*). Where complications developed a *B. fragilis* infection had been diagnosed at the time of surgery in 33 per cent of patients.

Forty-six of the patients received chemotherapy but in only 21 was the antibiotic given effective against bacteroides. Ten patients received either clindamycin or lincomycin, 5 tetracycline and the remainder either co-trimoxazole or metronidazole. Where ineffective treatment was prescribed 20 patients received ampicillin, 7 kanamycin, 4 cephaloridine and 3 co-trimoxazole. In several cases combined therapy was given.

Antibiotics were more commonly prescribed at the time of the operation when perforation of the intestine had occurred, but in many cases treatment was only given after the wound infection had developed.

In this retrospective analysis antibiotic therapy did not appear to improve the rate of recovery or reduce the incidence of complications.

The increase in the incidence of isolation of *B. fragilis* from postoperative wound infections following major intestinal surgery is shown in *Table IV*. Although the incidence of all wound infections rose only slightly between 1970 and 1973, the isolation rate of *B. fragilis* increased from 13 to 60 per cent. The increase in the isolation rate was due mainly to the use of special transport media which protected the bacteria present on the swab during delivery to the laboratory. In addition the swab was inoculated on to a special selective culture medium which contains neomycin to inhibit other bacteria.

Discussion

Infections due to *B. fragilis* occur most frequently after intestinal surgery (Gillespie and Guy, 1956), and in the Wycombe and Amersham Hospitals 67 per cent followed operations on the small and large bowel. In addition, where bacteroides organisms were isolated from abscesses 78 per cent of these had originated from the intestine. In this study the majority of wound infections followed appendicectomy, but this is probably only a reflection of the frequency of this operation.

All the wound infections were associated with severe inflammation, a purulent discharge and fever. There was frequent necrosis of the skin edges of the operative wound and in a few cases the suture line burst. Bacteria were isolated in large numbers and *B. fragilis* was always present in the highest count and was usually seen as the predominant organism in the Gram film. There was no clinical doubt that the wound was infected and not simply colonized in the superficial layers by bacteria.

B. fragilis was isolated in pure culture in nearly 50 per cent of the wound infections. In the past the incidence of sterile swabs from clinically infected wounds has been a common finding and there is little doubt that in many of these patients anaerobic bacteria which failed to grow on culture were responsible for the infection. The high incidence of *Klebsiella* spp. and *Enterobacter* spp. in mixed cultures (*Table II*) may be a reflection of previous antibiotic therapy as these organisms are resistant to ampicillin, an antibiotic commonly prescribed. Wound infection following surgery for malignant conditions of the intestine was usually caused by a single organism, and a mixed culture was found more frequently following perforation of the intestine.

The outcome of bacteroides infections is relatively good. Only 1 patient in this series died but 47 per cent of patients developed complications which prolonged their period of hospitalization. The commonest complication was metastatic abscess formation which frequently required further surgical intervention. The development of bacteriaemia is a serious feature of bacteroides infections which can increase the mortality to over 30 per cent (Bodner et al., 1970; Wilson et al., 1972; Leigh, 1974b), but this can be controlled by the early administration of effective antibiotic therapy (Gelb and Seligman, 1970; MacKenzie and Litton, 1974).

The role of antibiotic therapy in the prevention and treatment of wound infections after surgery is not generally known. Many antibiotic and antiseptic preparations have been used locally in the wound area to prevent infections (Crosfil et al., 1969; Longland et al., 1971; Gilmore et al., 1973; Evans et al., 1974). Parenteral antibiotic therapy has been shown to reduce the development of complications but not to influence wound healing (Magarey et al., 1971). However, in patients with perforated appendicitis the incidence of wound infection was reduced from 50 to 15 per cent when lincomycin was given early in the postoperative period (Leigh, 1974a). The success of antibiotic therapy depends on the activity of the chemotherapeutic agent against the infecting organisms and the dosage in providing adequate serum and tissue concentrations. Many studies have not prescribed antibiotics with significant bactericidal activity against anaerobic bacteria, and in the group of patients reported here less than 50 per cent received an antibiotic effective against bacteroides.

Bacteroides has an unusual spectrum of antibiotic susceptibility and it is rarely sensitive to the commonly prescribed chemotherapeutic agents. It is totally resistant to the aminoglycoside group of antibiotics such as gentamicin and kanamycin, and of the penicillins, only carbenicillin has consistent bactericidal activity because of the high blood levels that are achieved on standard parenteral therapy. Tetracycline has been used effectively in the past, but recent workers (Bodner et al., 1972; Kislak, 1972; Okubadejo et al., 1973) have found nearly 40 per cent of strains resistant to easily attainable serum concentrations. Clindamycin is the most active antibiotic against bacteroides and has been used with success in the treatment of infections (Bartlett et al., 1972), but it can only be given orally, and in severe infections parenteral lincomycin is the antibiotic of choice.

There are three main difficulties associated with the diagnosis of anaerobic infections following intestinal surgery. First, the failure of the surgeon to take specimens for bacteriological examination from areas of potential infection seen at operation. In appendicectomy it has been shown (Leigh, 1974a) that the isolation of *B. fragilis* from the appendix fossa is associated with a high incidence of wound infection, and that the administration of effective antibiotic therapy early in the postoperative period can reduce this incidence. Secondly, it is necessary to protect anaerobic bacteria which are highly oxygen-sensitive, and the specimen must be collected from deep in the wound and placed into a transport medium, either Stuart's or Robertson's meat broth, which provides an anaerobic environment. Many operations are performed outside the normal laboratory working hours and immediate examination and culture of the specimen are not possible.

In the laboratory it is always necessary to use selective media to isolate anaerobic bacteria, as it is time consuming and difficult to identify these bacteria amongst large numbers of aerobic organisms which may grow well even under anaerobic conditions. The increase in the isolation rate of *B. fragilis* when these precautions are taken is startlingly high (*Table IV*) and has confirmed the report of other workers (Hoffmann and Gierhake, 1969).

The incidence of wound infection following intestinal surgery is high; in the past it has been accepted as a natural sequel to the opening of the bowel and subsequent contamination of the peritoneal cavity and wound area. In the High Wycombe area in 1973, 15 per cent of patients undergoing major intestinal surgery developed a wound infection, and in 60 per cent *B. fragilis* was the causative organism either alone or in association with other bacteria. It is possible by bacteriological examination of the peritoneal cavity at the time of operation, especially in patients with perforation of the intestine where the incidence of wound infection is high, to diagnose the likely bacterial pathogens and to prescribe antibiotic treatment early in the postoperative period and prevent the subsequent wound infection. This procedure requires close cooperation between the surgeons and the laboratory, but it would be of great benefit to the patients in whom a wound infection may greatly delay their discharge from hospital.

In view of the high frequency of isolation of bacteroides from wound infections following intestinal surgery blind chemotherapy must include an antibiotic such as lincomycin which is effective against these organisms.

Acknowledgements

I would like to thank Mrs E. Norman, Control of Infection sister, who was responsible for the wound infection survey; the consultant surgeons, Mr P. H. Lord and Mr B. Higgs, for allowing the study of their patients; Mrs K. Simmons for the details of antibiotic susceptibility of the strains of bacteroides; and the technicians of the Microbiology Laboratory.

References

BARTLETT J. G., SUTTER V. L. and FINEGOLD S. M. (1972) Treatment of anaerobic infections with lincomycin and clindamycin. *New. Engl. J. Med.* **287**, 1006–1010.

BODNER S. J., KOENIG M. G. and GOODMAN J. S. (1970) Bacteremia bacteroides infections. *Ann. Intern. Med.* **73**, 537–544.

BODNER S. J., KOENIG M. G., TREANOR L. L. and GOODMAN J. S. (1972) Antibiotic susceptibility testing of Bacteroides. *Antimicrob. Agents Chemother.* **2**, 57–60.

COWAN S. T. and STEEL K. J. (1965) *Manual for the Identification of Medical Bacteria.* London, Cambridge University Press.

CROSFILL M., HALL R. and LONDON D. (1969) The use of chlorhexidine antisepsis in contaminated surgical wounds. *Br. J. Surg.* **56**, 906–908.

EVANS C., POLLOCK A. V. and ROSENBERG I. L. (1974) The reduction of surgical wound infections by topical cephaloridine: a controlled clinical trial. *Br. J. Surg.* **61**, 133–135.

GELB A. F. and SELIGMAN S. J. (1970) Bacteroidaceae bacteremia, effect of age and focus of infection on clinical course. *JAMA* **212**, 1038–1041.

GILLESPIE W. A. and GUY J. (1956) Bacteroides in intra-abdominal sepsis. *Lancet* **1**, 1039–1042.

GILMORE O. J. A., MARTIN T. D. M. and FLETCHER B. N. (1973) Prevention of wound infection after appendicectomy. *Lancet* **1**, 220–222.

GUNN A. A. (1956) Bacteroides septicaemia. *J. R. Coll. Surg. Edinb.* **2**, 41–50.

HOFFMANN K. and GIERHAKE F. W. (1969) Postoperative infection of wounds by anaerobes. *Ger. Med. Mon.* **14**, 31–33.

KISLAK J. W. (1972) The susceptibility of *Bacteroides fragilis* to 24 antibiotics. *J. Infect. Dis.* **125**, 295–299.

LEIGH D. A. (1974a) Bacterial flora of the appendix fossa and the incidence of wound infection. *J. Clin. Pathol.* **27**, 997–1000.

LEIGH D. A. (1974b) The clinical importance of infections due to *Bacteroides fragilis* and the role of antibiotic therapy. *Br. Med. J.* **3**, 225–228.

LONGLAND C. J., GRAY J. G., LEES W. and GARRETT J. A. M. (1971) The prevention of infection in appendicectomy wounds. *Br. J. Surg.* **58**, 117–119.

MACKENZIE I. and LITTON A. (1974) Bacteroides bacteriaemia in surgical patients. *Br. J. Surg.* **61**, 288–290.

MAGAREY C. J., CHANT A. D. B., RICKFORD C. R. K. and MAGAREY J. R. (1971) Peritoneal drainage and systemic antibiotics after appendicectomy. *Lancet* **2**, 179–182.

OKUBADEJO O. A., GREEN P. J. and PAYNE D. J. H. (1973) Bacteroides infection among hospital patients. *Br. Med. J.* **2**, 212–214.

WILSON W. R., MARTIN W. J., WILKOWSKE C. J. and WASHINGTON J. A. (1972) Anaerobic bacteraemia. *Mayo Clin. Proc.* **47**, 649–646.

the range is ours
the choice is yours

ETHICON
TRADEMARK
Eyeless needled sutures

QUALITY AND RELIABILITY AT EVERY STAGE

ETHICON* Eyeless Needled Sutures offer three outstanding advantages over traditional eyed needles.

Point 1 Consistent high quality—by precisely controlled manufacture of a complete sterile suture in a single package.

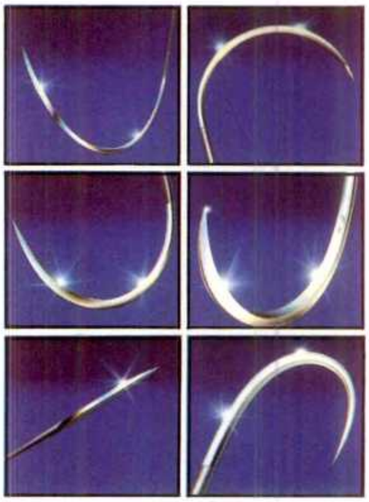
Point 2 A new sharp needle every time.

Point 3 Reduced trauma—with ETHICON eyeless needles there is no large eye and only one strand of material to pass through tissue.

The choice is yours

Most surgeons agree that there is no universal suture. Most probably there never will be. Each patient, each procedure, and each layer of tissue differs from the next. This is why we at ETHICON manufacture such a comprehensive range of eyeless needled sutures.

You can choose from our wide selection of materials, absorbable and non-absorbable, securely attached to a stainless steel needle of your choice. The consistent high quality of ETHICON eyeless needled sutures provides predictable performance. This enables you to concentrate on the most critical aspect of your surgery—the well-being of the patient.



We make
some very important points

Reduce Trauma

© ETHICON LTD 1974* Trade Mark

ETHICON
Eyeless needled sutures
Widest range. Finest quality

ETHICON Ltd., Bankhead Avenue, Edinburgh EH11 4HE, Scotland

PROLENE* Monofilament polypropylene for security you can count on

When the reliability of a non-absorbable is required in a contaminated or potentially contaminated field many surgeons are now choosing PROLENE suture. Made from polypropylene, a material of relative biological inertness, monofilament PROLENE suture is not degraded by tissue enzymes and is virtually unaffected by the presence of infection.

Security for extended approximation

Where wound healing may be delayed PROLENE suture can be relied on to retain its tensile strength.

Secure knot-holding

PROLENE suture is able to deform and flatten on knotting to give knot security superior to any other monofilament.

Security through reduced risk of suture extrusion and sinus formation

The specially smooth monofilament structure of PROLENE suture and its ability to tolerate infection extremely well can lessen the risk present with a braided suture in a contaminated wound.

Indications: PROLENE Polypropylene suture may be used wherever a non-absorbable surgical suture is recommended.

Precautions: Unused PROLENE sutures may not be autoclaved more than three times by the standard autoclaving method without loss of strength. Care should be taken to avoid damaging the surface of the material with surgical instruments.

ETHICON

TRADEMARK

Widest range. Finest quality

© ETHICON LTD 1974* Trade Mark

ETHICON LTD. Bankhead Avenue, Edinburgh EH11 4HE, Scotland.

Br. J. Surg. Vol. 62 (1975) 379–382

Pneumatosis cystoides intestinalis with unexplained ascites in Ethiopian patients

EDEMARIAM TSEGA

SUMMARY

Four cases of pneumatosis cystoides intestinalis associated with unexplained ascites in Ethiopian patients are described. The relationship between the two conditions has not previously been reported.

PNEUMATOSIS cystoides intestinalis (PCI) is an uncommon condition characterized by multiple gas-filled thin-walled cysts of the subserosal and submucosal layers of the intestine. It was first described by DuVernoi in 1730 (quoted by McGregor and McKinnon, 1958), the first detailed report was published by Bang (1876) but the first radiological description was provided by Englund and Wahlgren (1935). In a review of 213 cases Koss (1951) reported that the small bowel was affected in 63 per cent and the large bowel in 22 per cent of cases, the former being commonly associated with gastric or duodenal ulcers. PCI almost invariably occurs in patients suffering from other conditions, mainly of gastro-intestinal or pulmonary origin. Reported associated gastro-intestinal lesions include pyloric stenosis, duodenal ulcer, gastric ulcer or carcinoma, regional enteritis, various forms of colitis, tuberculosis and obscure forms of diarrhoea. PCI also occurs in the presence of chronic pulmonary disease (Doub and Shea, 1960; Keyting et al., 1961; Kenney, 1963). Other conditions associated with PCI include acute leukaemia (Jaffe et al., 1972), lymphoproliferative disorders (Mujahad and Evans, 1958; Williams et al., 1963), progressive systemic sclerosis (Gompels, 1969) and malnutrition (Druckmann et al., 1961).

The purpose of this paper is to describe 4 patients with PCI in whom unexplained ascites was found, a relationship not reported previously in the English literature.

Case reports

Case 1: H. H., a 26-year-old merchant, was admitted to hospital for treatment of a crush injury of the right foot. He also gave a 3-year history of intermittent vomiting of undigested foodstuff preceded by uncomfortable abdominal distension, especially after meals. He had anorexia and marked undetermined weight loss. There was no definite epigastric pain, cough, fever, night sweats or history of jaundice or drug intake.

On examination the patient was noted to be emaciated, pale and chronically ill. His blood pressure was 100/70 mm Hg and his pulse was 100/min. The respiratory and cardiovascular systems were normal. The abdomen was distended, with flank dullness and fluid thrill. No intra-abdominal organs could be palpated. Rectal examination was normal.

Red blood cell count was $2 \times 10^6/\text{mm}^3$ and the ESR 120 mm in the first hour. A Mantoux skin test with 2 units of PPD was negative. The urinalysis and blood urea nitrogen were normal. The liver function tests, including bromsulphthalein, were within normal limits. A bone marrow aspirate was normal and negative for acid-fast bacilli. Diagnostic paracentesis yielded clear yellow fluid containing 500 WBC/mm^3 of which 90 per cent were lymphocytes, with a protein content of 3·5 g/l and no growth of *Mycobacterium tuberculosis* after 6 weeks of incubation. A barium meal examination showed enormous dilatation of the stomach which almost filled the abdomen, and from which no barium had passed after 2 hours.

At exploratory laparotomy approximately 1500 ml of straw-coloured, ascitic fluid were removed. The stomach was dilated to almost four times the normal size but there was no evidence of a gastric lesion or duodenal ulcer. However, the first part (4 cm) of the duodenum was found to be very narrow, with a lumen barely sufficient to allow the passage of a lead pencil, but with no thickening or scarring of the wall. The liver, biliary tree, peritoneum, omentum, pancreas and terminal ileum were all normal. The lower jejunum and upper ileum were noted to have multiple subserosal gas-filled cysts, characteristic of PCI. After an operative diagnosis of congenital stenosis of the duodenum in an adult, a Billroth II anastomosis was performed. The narrow duodenum was removed together with the stomach, but no histological report was obtained.

Four months after operation the patient had no ascites or any symptom and he had gained much weight.

Case 2: M. K., a 14-year-old girl, was admitted to hospital with a history of long-standing recurrent abdominal distension which had suddenly become worse 4 months prior to admission. A month before admission she had experienced a stabbing pain in the right upper quadrant of the abdomen, radiating to the right shoulder and aggravated by deep breathing. There was no history of chronic cough, epigastric pain, vomiting, diarrhoea or jaundice.

On physical examination the vital signs, lungs and cardiovascular systems were within normal limits. The abdomen was markedly distended and tympanitic to percussion over the upper quadrants. The liver dullness was decreased. There was flank fullness and dullness; no intra-abdominal organ or mass could be palpated. The presumptive clinical diagnosis at admission was tuberculous peritonitis.

A plain film of the abdomen in the upright and supine positions revealed pneumoperitoneum and cystic gas collections in the right upper quadrant (*Fig.* 1). A chest X-ray showed normal lungs and air under the right diaphragm. A barium meal study showed downward displacement of the stomach and rapid transit of the barium from the stomach to the small intestine. Barium enema examination and sigmoidoscopy were unrevealing. Haematological and biochemical tests, including liver function tests, demonstrated normal findings. A diagnostic paracentesis revealed straw-coloured fluid with a specific gravity of 1010, protein of 1·64 g per cent, total WBC of 500/mm^3 (69 per cent lymphocytes, 29 per cent neutrophils and 2 per cent oesinophils) and a negative reaction to Gram and Ziehl–Neelsen stains.

At an exploratory laparotomy the presence of air in the intra-abdominal cavity was apparent. Multiple air-filled subserosal cysts were seen from the lower part of the jejunum down to the terminal ileum. About 1500 ml of straw-coloured ascitic fluid were removed. The liver, spleen, pancreas, stomach and duodenum were normal. Biopsies were taken from the omentum, the serosal layer of the small intestine and lymph nodes adjacent to the mesentery. The cysts were described as empty sacs lined with flattened endothelial cells compatible with PCI. No other abnormality was seen.

---

* St Paul's Hospital, Haile Sellassie I University, Addis Ababa, Ethiopia.

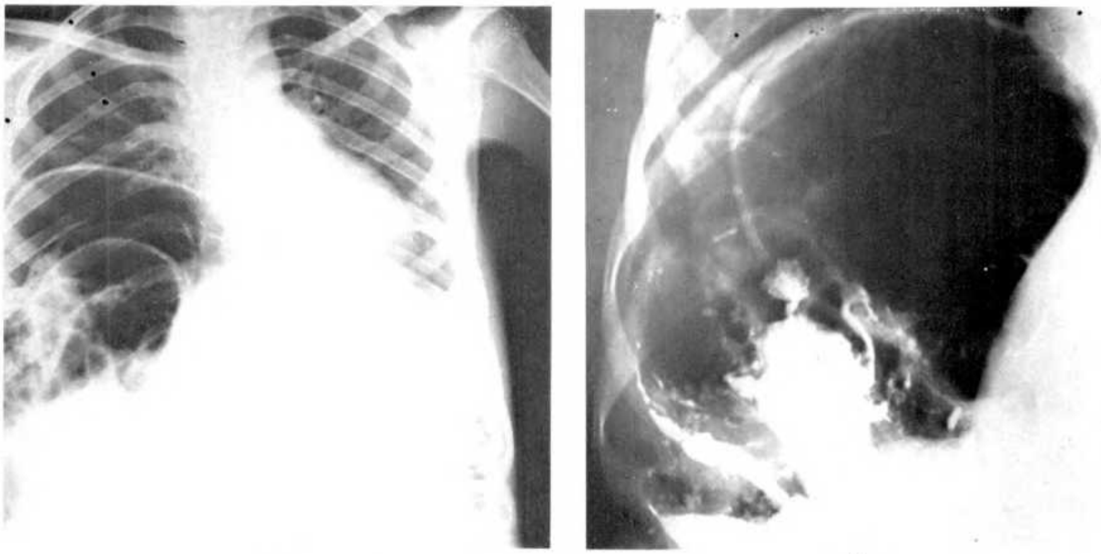

a *b*

Fig. 1. *Case* 2. *a*. Pneumoperitoneum and cystic gas collections in the right upper quadrant of the abdomen. *b*. Magnified right upper quadrant.

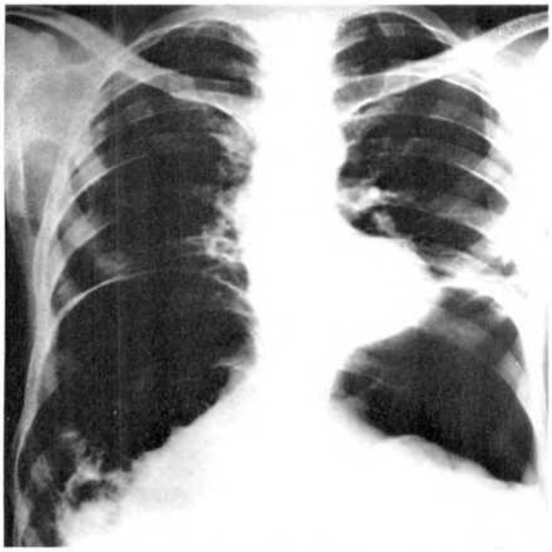


Fig. 2. *Case* 4: Chest X-ray showing pneumoperitoneum.

Follow-up 3 months after operation revealed recurrence of symptoms but without ascites. There was again air under the right diaphragm. A repeat barium meal with fluoroscopy showed retention of contrast medium in the stomach for 24 hours, and there were cystic structures which changed in size with respiration and appeared about to rupture at any moment. A diagnosis of recurrent pneumoperitoneum from ruptured PCI was made.

Case 3: A. T., an 18-year-old man, had had an abrupt attack of weakness and giddiness, followed by massive haematemesis some 6 years prior to admission. Soon after this episode he had begun to experience cramp-like and burning epigastric pain, which continued throughout the 6 years, with a certain degree of rhythmicity and periodicity, often occurring 2 hours after meals and waking him up at 1 or 2 a.m. For the past 2–3 years, he had had postprandial distension, often relieved by either spontaneous or self-induced vomiting. The vomitus had sometimes contained food material ingested 24 hours previously.

Physical examination revealed a thin and undernourished man with flank fullness, shifting dullness and succussion splash several hours after his last meal. There was no other finding.

A barium meal study showed an enlarged and hypotonic stomach with flattened mucosa and with 50 per cent of the barium still present 27 hours later. Haematological and biochemical tests, including liver function tests, revealed normal findings. The clinical impression was benign pyloric obstruction.

At laparotomy 2000 ml of clear ascitic fluid were removed. Extensive gas-filled subserosal cysts were noted extending from the middle of the jejunum to the terminal ileum and a few were seen on the mesentery; a biopsy confirmed the operative impression of PCI. The pylorus was said to be normal by the surgeon. There was no other abnormality.

Six weeks after operation the patient began to complain again of abdominal distension and vomiting. There was no evidence of ascites at this time. A repeat barium meal examination was again suggestive of pyloric obstruction. Gastroscopy revealed a large distensible stomach, flattened mucosa and prominent veins in the antrum. There was no ulcer but the pyloric region revealed a tear-drop type deformity. A second exploratory laparotomy was suggested but the patient refused and discharged himself from hospital.

Case 4: T. W. T., a 42-year-old man, was admitted to hospital with burning epigastric pain and recurrent vomiting after meals. He had weighed 65 kg at one time but was only 39 kg at the time of admission.

On physical examination the patient appeared emaciated, pale, dehydrated and chronically ill, with a blood pressure of 90/70 mm Hg. The respiratory and cardiovascular systems were normal. The abdomen was moderately distended with flank fullness and shifting dullness. There was a succussion splash in the epigastrium several hours after the last meal. The rest of the physical examination was unrevealing.

A chest X-ray demonstrated air under the right diaphragm (*Fig*. 2) and a barium meal film showed a huge stomach with prolonged retention of barium and displacement of the intestine and the colon downwards. The gastric aspirate after an overnight fast was 1400 ml. The haematocrit was 36 per cent and the stool showed occult blood (+ + +). The ESR was 60 mm in the first hour. The serum blood urea nitrogen was 102 mg per cent at the time of admission but decreased to 32 mg per cent after rehydration. The liver function tests were normal.

At laparotomy pneumoperitoneum was evident. More than 3 litres of straw-coloured ascitic fluid were removed from the peritoneal cavity. There were multiple grape-like clusters of gas-filled cysts of varying size studding the subserosal surface of almost the entire small bowel. A complete pyloric stenosis was found and treated with gastrojejunostomy. No other abnormality was detected. The patient did well postoperatively, and has not returned for follow-up since his discharge.

Discussion

Although PCI is said to be rare, more than 300 cases have been reported. It seems that the condition is more common than was previously thought (Elliott and Elliott, 1963; Smith and Welter, 1967). It is often diagnosed at operation or at autopsy but seldom clinically or radiologically. The disease occurs about three times more frequently in males than females (Koss, 1952). The majority of cases are within the age group of 20–50 years. However, there are isolated reports of infants and children who were found to have PCI with or without associated intestinal conditions (Stiennon, 1951; McGregor and McKinnon 1958; Swerdlow, 1964; Smith and Welter, 1967).

The clinical features of PCI include constipation, flatulence, distension, vomiting, vague abdominal pain, diarrhoea and occasionally frank bleeding. Often, most of these symptoms resolve spontaneously. In some cases the associated conditions mask the clinical picture. Intestinal obstruction, pneumoperitoneum, volvulus (Jones, 1948), perforation and prolapse of cysts through the anus (Wyatt, 1972) may rarely occur as complications. Intestinal obstruction results from bulging submucosal cysts (common in children), while pressure exerted by cysts on veins may cause occlusion and subsequent bowel infarction, perforation and peritonitis.

Many cases of PCI remain asymptomatic and are best managed conservatively. Complications such as obstruction, volvulus or adhesion, however, require surgical intervention. Most cases resolve after surgical treatment of the associated or underlying condition, e.g. pyloric stenosis.

One striking feature common to all of the subjects described here is the significant amount of ascites which did not recur after removal at laparotomy and for which no apparent cause could be found. Liver biopsies were not done but the liver function tests and the gross appearances of the livers at surgery were normal in all the cases. Ascites is not a feature of duodenal ulcer or obstruction. There was no apparent cardiac, renal or gastro-intestinal cause. Tuberculous peritonitis was excluded in *Cases* 1 and 2. Surgical exploration has excluded the possibility of the extra-hepatic portal hypertension that may be caused by chronic pancreatitis (Longstreth et al., 1971) or portal vein obstruction. The aetiology of the ascites therefore remains unexplained.

A second interesting finding was pneumoperitoneum, which is a rare complication of PCI (*Cases* 2 and 4). This is usually the result of a spontaneous rupture of subserosal cysts. Silent pneumoperitoneum, sometimes massive, long-standing and recurrent, associated with PCI and without peritonitis has been reported (Druckmann et al., 1961; Elliott and Elliott, 1963). *Case* 2 is a good example of this.

The number of conditions described as being associated with PCI continues to increase but the exact mechanism of cyst formation remains poorly understood. Of several theories proposed, two are generally accepted, viz. mechanical and pulmonary. The mechanical theory maintains that gas from the lumen of the intestine gains access to the tissues through the epithelial wall. This seems likely in duodenal and gastric ulcer, gastric carcinoma, regional enteritis, colitis, neoplastic infiltration of the bowel, following colostomy (Hall, 1971) and trauma secondary to sigmoidoscopy (Marshak et al., 1956). Also, the high percentage of hydrogen in the gas content of the cysts (nitrogen 72·5 per cent, hydrogen 10·1 per cent, oxygen 7·0 per cent, carbon dioxide 1·7 per cent, etc., measured by Hughes et al., 1966) suggests that gas diffuses into the cysts from the bowel, probably under pressure. However, the absence of PCI in most bowel diseases that give rise to mucosal damage and its occurrence without intestinal disease suggest that the mechanical theory does not account for all cases of PCI. The pulmonary theory advocates that ruptured alveoli lead to pneumomediastinum from which air travels along the sheaths of the pulmonary arteries which are in continuity with the fascial sheath of the aorta and its branches and eventually to the walls of the intestine (Doub and Shea, 1960; Keyting et al., 1961; Elliott and Elliott, 1963). Plachta and Speer (1961) and Keyting et al. (1961) have shown experimentally that air will track along the aorta from the mediastinum, and that injection of air into the tissue surrounding the root of the inferior mesenteric artery results in colonic lesions similar to human PCI. However, not all cases of pneumomediastinum give rise to PCI and it is a rare finding among patients with chronic obstructive lung disease. Neither theory accounts for the PCI described either in cases with malnutrition (Druckmann et al., 1961; Jaffe et al., 1972) or in cases without other known disease (Swerdlow, 1964). It would be interesting to know the actual incidence of PCI in the tropics where the prevalence of malnutrition and intestinal parasites is very high.

A striking feature common to 3 of the 4 cases presented here was gross gastric dilatation. *Case* 1 was found to have an organic cause which was surgically corrected and no further trouble occurred. Unfortunately, *Case* 4 did not return for follow-up. In *Case* 2, although the first barium meal showed rapid gastric emptying, a repeat barium study at the time of recurrence of her symptoms revealed significant stasis in the stomach. It is difficult to explain this apparent association between gastric dilatation and PCI, and none of the suggested theories explains the formation of gross ascites in each of the 4 cases. Therefore, the cause of PCI and its relationship to other conditions, including ascites, require further studies.

Acknowledgements

I am grateful to Dr D. Obradovic of St Paul's Hospital and to Drs H. Friedrichs and Adugna Makonnen of Haile Sellassie I Hospital for their surgical assistance.

I thank Dr F. T. Lester of Haile Sellassie I Hospital for permission to report *Cases* 1 and 4. I am indebted to Mr Zewdu Kebede of the Department of Audiovisual Aid, Haile Sellassie I University, for the photographs.

References

BANG B. L. F. (1876) Luftholdige kyster i väggen af ileum og i nydannet bindeväz pa sammes serosa. *Nord. Med.* **8**, 1. (Quoted by MCGREGOR J. K. and MCKINNON D. A., 1958.)

DOUB H. P. and SHEA J. J. (1960) Pneumatosis cystoides intestinalis. *JAMA* **172**, 1238–1242.

DRUCKMANN A., SCHWARTZ A., RABINOVICI N. and FEUCHTWANGER M. (1961) Pneumatosis of the intestines. *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **86**, 911–919.

ELLIOTT G. B. and ELLIOTT K. A. (1963) The roentgenologic pathology of so-called pneumatosis cystoides intestinalis. *Am. J. Roentgenol. Radium. Ther. Nucl. Med.* **89**, 720–729.

ENGLUND F. and WAHLGREN F. (1935) Fall von Pneumatosis cystoides intestinorum bein Menschen. *Acta Chir. Scand.* **76**, 607–614.

GOMPELS B. M. (1969) Pneumatosis cystoides intestinalis. *Br. J. Radiol.* **42**, 701–703.

HALL R. (1971) Delayed tension pneumoperitoneum after colostomy closure. *Br. J. Surg.* **58**, 574–576.

HUGHES D. T. D., GORDON K. C. D., SWANN J. C. and BOLT G. L. (1966) Pneumatosis cystoides intestinalis. *Gut* **7**, 553–557.

JAFFE N., CARLSON D. H. and VAWTER G. F. (1972) Pneumatosis cystoides intestinalis in acute leukemia. *Cancer* **30**, 239–243.

JONES J. D. T. (1948) Gas cysts of intestine. *Br. J. Surg.* **36**, 49–50.

KENNEY J. G. (1963) Pneumatosis intestinalis. *Clin. Radiol.* **14**, 70–76.

KEYTING W. S., MCCRAVER R. R., KOVARIK J. L. and DAYWITT A. L. (1961) Pneumatosis intestinalis: new concept. *Radiology* **76**, 733–741.

KOSS L. G. (1951) Abdominal gas cysts (pneumatosis cystoides intestinorum hominis). *Arch. Pathol.* **53**, 537–549.

KOSS L. G. (1952) Abdominal gas cysts (pneumatosis cystoides intestinorum hominis); analysis with report of case and critical review of literature. *Arch. Pathol.* **53**, 523–549.

LONGSTRETH G. F., NEWCOMER A. D. and GREEN P. A. (1971) Extrahepatic portal hypertension caused by chronic pancreatitis. *Ann. Intern. Med.* **75**, 903–908.

MCGREGOR J. K. and MCKINNON D. A. (1958) Intestinal interstitial emphysema (pneumatosis cystoides intestinalis). *Gastroenterology* **35**, 206–211.

MARSHAK R. H., BLUM S. D. and ELIASOPH J. (1956) Pneumatosis involving the left side of the colon. *JAMA* **161**, 1626–1628.

MUJAHED Z., and EVANS J. A. (1958) Gas cysts of the intestine: pneumatosis intestinalis. *Surg. Gynecol. Obstet.* **107**, 151–160.

PLACHTA A. and SPEER F. D. (1961) Mechanism of nonbacterial gastric emphysema. *Gastroenterology* **40**, 248–252.

SMITH B. H. and WELTER L. H. (1967) Pneumatosis intestinalis. *Am. J. Clin. Pathol.* **48**, 455–465.

STIENNON O. A. (1951) Pneumatosis intestinalis in newborn. *Am. J. Dis. Child.* **81**, 651–663.

SWERDLOW H. (1964) Pneumatosis cystoides intestinalis: characteristics and report of four cases. *Dis. Colon Rectum* **7**, 306–308.

WILLIAMS M. J., SUTHERLAND D. H. and CLARK C. G. (1963) Lymphosarcoma of the small intestine with a malabsorption syndrome and pneumatosis intestinalis. Report of a case with peroral jejunal biopsy. *Gastroenterology* **45**, 550–557.

WYATT A. P. (1972) Pneumatosis cystoides intestinalis. *Proc. R. Soc. Med.* **65**, 780–782.

Br. J. Surg. Vol. 62 (1975) 383–386

Caecal rupture due to colonic ileus

EUGENE D. GIERSON, F. KRISTIAN STORM, WILLIAM SHAW AND SUSAN K. COYNE*

SUMMARY

Caecal rupture due to colonic ileus is rare and has a mortality rate of 43 per cent. Three new cases are presented and the 18 previously reported cases are reviewed. The disease has always occurred in association with another illness, has usually afflicted patients over the age of 55 and has only resulted when the caecum was at least 9 cm in diameter. The technique of 'blow-hole' caecostomy, a method for decompressing the distended caecum, is described.

CAECAL rupture due to colonic ileus is an unusual complication of pseudo-obstruction of the colon (Ogilvie's syndrome). It is often fatal and is sufficiently rare that we could find only 18 cases in the literature. Low and Fairly reported the first case in 1934, but they failed to recognize the syndrome, probably because ileus of the colon was unknown until Ogilvie's paper in 1948. In 1958 Robertson et al. (unaware of the article by Low and Fairly) claimed the first report, and in 1973 Wojtalik et al. collected 12 cases from the literature and added 3 of their own.

The purpose of our paper is to report 3 cases of caecal rupture due to colonic ileus and to describe the technique of 'blow-hole' caecostomy.

Case reports

Case 1: A 69-year-old man with a long history of peptic ulcer disease was admitted to Sepulveda Veterans Administration Hospital with a diagnosis of perforated duodenal ulcer of 20 hours' duration. The perforation was oversewn shortly after admission. One week later a small leak from the duodenum was treated by coeliotomy and drainage. The patient's postoperative course was complicated by pneumonia, upper gastro-intestinal bleeding, candidaemia associated with hyperalimentation and acute renal failure. Six weeks after the initial operation he developed right lower quadrant abdominal pain and tenderness. Abdominal X-rays showed a dilated caecum, 14 cm in diameter. Gastrografin enema showed no obstruction and no leak. However, 5 days later an X-ray revealed free air in the abdomen with decompression of the caecum. At operation a caecal perforation and diffuse peritonitis were found. Tube caecostomy was performed, using a mushroom catheter, size 26 French. Postoperatively, caecostomy drainage was poor, and 1 week later coeliotomy was done to replace the caecostomy tube and to drain a subphrenic abscess. The patient developed renal failure, pneumonia and hyperbilirubinaemia. Faecal drainage around the caecostomy tube caused peritonitis and sepsis. The patient died of sepsis 20 days after the caecum had perforated.

Case 2: A 59-year-old male was admitted to UCLA Hospital because of weakness and dyspnoea for 2 months. Chest X-ray films revealed an abscess cavity in the left lung and pulmonary emphysema. Incision and drainage of the pulmonary abscess were performed on the day following admission. Postoperatively the patient did poorly. His course was complicated by sepsis, respiratory deterioration, leucopenia and abdominal distension which slowly progressed. On the sixteenth postoperative day abdominal X-ray showed the caecum to be 'markedly distended'. An exploratory coeliotomy revealed two large caecal perforations and no obstruction of the colon. A right colectomy with ileostomy and mucous fistula was done. Postoperatively the patient had sepsis and he died on the day after operation.

Case 3: A 76-year-old female had been asymptomatic for 1 year following a transverse colostomy for diverticulitis. She was admitted to UCLA Hospital because of pain for 2 days in the right lower quadrant of the abdomen. Abdominal distension was present, bowel sounds were active and the right lower quadrant was tender. X-ray films revealed an ileus pattern with a dilated caecum. After 20 hours of observation a barium enema X-ray study was done. It showed extravasation from the caecum into the free peritoneal cavity and no evidence of obstruction. Coeliotomy revealed perforation of an ulcerated necrotic area of the caecum with barium peritonitis. Right colectomy with primary ileocolostomy was performed. Postoperatively, the patient had sepsis and she died on the sixth postoperative day. At autopsy the absence of colonic obstruction was confirmed.

Discussion

Table I summarizes the cases reported in the literature as well as our cases. There are a total of 21 cases, and most of the patients were over 55 years. In each case there was an associated major illness or trauma, or the patient had had recent surgery. Apart from the fact that there was an associated disease of some sort, no consistent pattern was discernible. Diagnosis was established when symptoms and signs of an abdominal catastrophe led to coeliotomy. Preoperative X-rays were not reliable for determining perforation; free intraperitoneal air was absent in one-half of the cases and barium enema studies showed a similar rate of error. The caecal diameter was always 9 cm or larger, ranging from 9 to 20 cm. The operation most frequently performed was tube caecostomy, with a 20 per cent mortality. Overall, the mortality rate was 43 per cent and hospital stay averaged 6·8 weeks for surviving patients. Moreover, in excess of 60 per cent of patients suffered major postoperative complications, including evisceration, stress ulcer, peritonitis and abdominal abscesses. Thus, even for survivors this was a disastrous illness.

How can the caecum perforate in the absence of distal obstruction? We propose the following sequence. A disease process not involving the bowel results in an imbalance of sympathetic and parasympathetic activity (Ogilvie, 1948; Dunlop, 1949; MacFarlane and Kay, 1949; Wanebo et al., 1971). Colonic peristalsis ceases.

---

* UCLA Medical Centre, Los Angeles, and Department of Surgery, Sepulveda Veterans Administration Hospital, Sepulveda, California.

Present address of Eugene D. Gierson, Southern California Permanente Medical Group, 1050 West Pacific Coast Highway, Harbor City, California 90710.

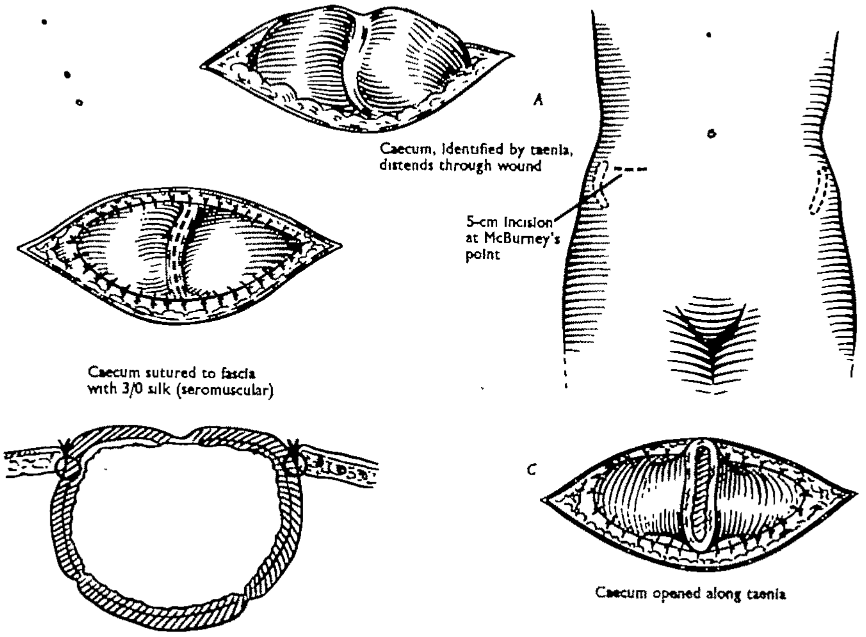

A
Caecum, identified by taenia, distends through wound
5-cm incision at McBurney's point
Caecum sutured to fascia with 3/0 silk (seromuscular)
C
Caecum opened along taenia

Fig. 1. Technique of 'blow-hole' caecostomy.

Table I: REPORTED CASES OF CAECAL RUPTURE DUE TO COLONIC ILEUS

Author	Age	Sex	Associated illness	Symptoms and signs	Duration of symptoms (d)	Caecal diameter (cm)	Free air in abdomen	Operation	Resul
Low and Fairley (1934)	58	F	Tropical sprue	Pain, distension	<1	—	—	Laparotomy	Died
Eckman et al. (1958)	75	F	Rib/shoulder fixation	Distension	13	9	Yes	None	Died
Robertson et al. (1958)	25	F	C-section	Distension	3	15	—	Tube caecostomy	Alive
Morton et al. (1960)	74	M	Pneumonia	Pain, distension	5	Widely dilated	—	Caecostomy and transverse colostomy	Alive
	39	M	Urinary sepsis	Pain, distension	<1	Greatly dilated	No	Tube caecostomy	Alive
Hirsch (1961)	41	F	Difficult delivery	Pain, distension	2	—	—	Primary repair	Alive
Millar and Ovlisen (1966)	24	F	C-section	Pain, ileus	7	—	Yes	Caecostomy*	Alive
	35	F	C-section	Pain, ileus	7	—	—	Caecostomy*	Died
Dumont and Dovy (1967)	23	F	C-section	Distension	3	—	—	Caecostomy*	Alive
Yeo (1967)	73	M	Inguinal herniorrhaphy	Distension	8	14	Yes	Tube caecostomy	Alive
	64	M	Nephrectomy	Distension	8	—	Yes	Caecostomy*	Alive
Carrasquilla et al. (1970)	79	M	Inguinal herniorrhaphy	Tender, distension	4	20	No	Repair, tube appendicostomy	Alive
	62	F	Femur fracture	Tender, ileus	3	14	No	Exteriorization	Died
	62	M	Pulmonary tuberculosis, gastro-intestinal bleed	Pain	3	—	Yes	Caecostomy*	Alive
Muggia (1972)	56	M	Cirrhosis, hypokalaemia	Ileus	1	19	Yes	Caecostomy*	Alive
Wojtalik et al. (1973)	67	M	Pancreatitis	Distension	1	12	No	Tube caecostomy	Died
	45	M	Cervical myelitis	Distension	3	12	No	Right colectomy	Died
	49	F	Tibia fracture	Tender, distension	<1	15	Yes	Caecostomy*	Alive
Present series (1975)	69	M	Duodenal ulcer operation, ATN	Pain, distension	5	14	Yes	Tube caecostomy	Died
	59	M	Lung abscess drainage	Distension	11	Markedly distended	No	Right colectomy	Died
	76	F	Diverticulitis	Pain	2	—	No	Right colectomy	Died

* Presumed to be tube caecostomy though not stated in report.

Gas accumulates due to swallowed air, bacterial by-products and gas from the bloodstream, entering the gut lumen by diffusion (Wangensteen, 1955). Normally, gas is carried away by the motility of the colon and by bloodstream absorption, but in the face of an ileus, distension progresses and is most severe in the caecum because of its weak wall. Increasing distension impedes blood flow, causing necrosis of the caecal wall and perforation. An incompetent ileocaecal valve does not guarantee against caecal rupture (Eckman et al., 1958; Robertson et al., 1958).

With a mortality rate of 43 per cent, prevention of caecal perforation is important. In turn, prevention requires the ability to predict in advance which caecum will rupture. This seems to be related to caecal diameter, perforation having occurred only if the diameter had reached at least 9 cm. Moreover, the normal caecum is less than 9 cm (Davis and Lowman, 1957). We therefore propose the 'rule-of-nine': a caecum distended to 9 cm is in danger of perforating. This circumstance requires careful therapy. We think it safest to perform 'blow-hole' caecostomy (described below), but if non-operative therapy is elected the patient should be observed closely.

The operation to create a 'blow-hole' caecostomy is sufficiently simple and safe that it can be done using local anaesthesia. After surgery one can be confident that the caecum will remain decompressed, and the problems of a tube caecostomy are avoided. Such problems include occlusion of the catheter by faeces, spillage of faeces into the abdominal cavity and postoperative recurrent caecal rupture. Tube caecostomy has failed in up to 50 per cent of cases and has been condemned by many (Gregg and Dixon, 1941; Hendricks and Griffin, 1947; Michel and McCafferty, 1948; Albers and Smith, 1952; Hunt, 1954; Rack and Clement, 1954; Maynard and Turell, 1955). Moreover, inadequate function of the tube can be fatal (Jackson and Baird, 1967; Hopkins, 1969; Balslev et al., 1970; Norton et al., 1974). Although many reports have been unfavourable, Wanebo et al. (1971) reported good results in 4 patients. When complications of tube caecostomy do occur they are so disastrous that we recommend avoiding the tube entirely and using the 'blow-hole' technique instead.

Technique of 'blow-hole' caecostomy (*Fig.* 1)

Local 0·25 per cent lidocaine (Xylocaine) with epinephrine (Gierson, 1972) or light general anaesthesia is used. A 5-cm transverse incision is made 5 cm cephalad to the right anterior superior iliac spine, lateral to the rectus muscle. The internal oblique, external oblique and the transversalis muscles may be split or cut. It is important to remain lateral to the rectus muscle to ensure that the caecum is encountered and not the small bowel. The distended caecum will 'pop' into the wound and is identified by the presence of taeniae. It is desirable to have a portion of the caecum protrude above the skin, as this facilitates placement of a colostomy bag.

The seromuscular layers of the caecum are sutured to the external or internal oblique muscles, care being taken to include the aponeurosis of these muscles in each suture; 3/0 silk sutures, swaged on to a gastrointestinal needle, are used. Care is taken not to penetrate the mucosa of the bowel. These interrupted sutures are placed circumferentially, and closely spaced to ensure a watertight seal. If there is doubt that a watertight seal has been achieved, a second layer of sutures is placed, joining the caecal wall to the subcutaneous fat (Turnbull et al., 1971).

The caecum is incised with a scalpel through the taenia or through a lateral-inferior area. Large quantities of gas and faeces will spill out. A lateral-inferior incision facilitates gravity drainage into the subsequently placed colostomy bag. Cautery should not be used, as explosion may result (Barrkman, 1965; Ragins et al., 1974). Bleeding of the cut edges of the caecostomy is controlled by clamp and silk ligature. The skin is not closed.

Acknowledgements

The authors wish to acknowledge the secretarial assistance of Miss Evelyn M. Gibson and Mrs Brenda Perdue.

References

ALBERS J. H. and SMITH L. L. (1952) A comparison of cecostomy and transverse colostomy in complete colon obstruction. *Surg. Gynecol. Obstet.* **95**, 410–415.

BALSLEV I., JENSEN H. and NIELSEN J. (1970) The place of cecostomy in the relief of obstructive carcinoma of the colon. *Dis. Colon Rectum* **13**, 207–210.

BARRKMAN M. F. (1965) Intestinal explosion after opening a caecostomy with diathermy. *Br. Med. J.* **1**, 1594–1595.

CARRASQUILLA C., ARBULU A., FROMM S. and LUCAS C. (1970) Cecum perforation due to adynamic ileus. *Dis. Colon Rectum* **13**, 252–254.

DAVIS L. and LOWMAN R. (1957) Roentgen criteria of impending perforation of the cecum. *Radiology* **68**, 542–547.

DUMONT M. and DOVY D. (1967) Perforation spontanée du caecum après césarienne. *Rev. Fr. Gynécol. Obstet.* **62**, 531–533.

DUNLOP J. A. (1949) Ogilvie's syndrome of false colonic obstruction: a case with post-mortem findings. *Br. Med. J.* **1**, 890–891.

ECKMAN W. G., WENZKE F. and ABRAMSON W. (1958) Perforation of the cecum complicating adynamic ileus. *Am. J. Surg.* **96**, 718–720.

GIERSON E. D. (1972) Vasoconstrictor agents in local anaesthetic preparations. *Lancet* **2**, 1142.

GREGG R. O. and DIXON C. F. (1941) Operable malignant lesions of the colon producing obstructions. *Surg. Clin. North Am.* **21**, 1143–1145.

HENDRICKS W. and GRIFFIN W. D. (1947) Symposium on clinical advances in surgery: intestinal obstruction. *Surg. Clin. North Am.* **27**, 51.

HIRSCH M. I. (1961) Spontaneous rupture of the cecum: report of a case. *Cent. Am. J. Med.* **7**, 49.

HOPKINS J. E. (1969) Tube cecostomy: an appraisal. *Dis. Colon Rectum* **12**, 379–385.

HUNT C. J. (1954) Surface cecostomy as a procedure for the decompression of the acutely obstructive colon. *Am. Surg.* **20**, 1062–1069.

JACKSON P. P. and BAIRD R. M. (1967) Cecostomy: an analysis of 102 cases. *Am. J. Surg.* **114**, 297–301.

LOW G. C. and FAIRLEY N. H. (1934) Fatal perforation of the cecum in a case of sprue. *Br. Med. J.* **2**, 678–679.

MACFARLANE J. A. and KAY S. K. (1949) Ogilvie's syndrome of false colonic obstruction: is it a new clinical entity? *Br. Med. J.* **2**, 1267–1269.

MAYNARD A. D. and TURELL R. (1955) Acute left colon obstruction with special reference to cecostomy versus transversostomy. *Surg. Gynecol. Obstet.* **100**, 667–674.

MICHEL M. L. and MCCAFFERTY E. L. (1948) Acute obstruction of the colon with special reference to factors of mortality. *Arch. Surg.* **57**, 774–779.

MILLAR D. R. and OVLISEN B. (1966) Two cases of spontaneous perforation of the caecum following caesarean section. *Acta Obstet. Gynecol. Scand.* **45**, 254–259.

MORTON J. H., SCHWARTZ S. I. and GRAMIAK R. (1960) Ileus of the colon. *Arch. Surg.* **81**, 425–434.

MUGGIA A. L. (1972) Perforation of the cecum associated with hypokalemic ileus. A report of a case. *Am. J. Gastroenterol.* **57**, 169–171.

NORTON L., YOUNG D. and SCRIBNER R. (1974) Management of pseudo-obstruction of the colon. *Surg. Gynecol. Obstet.* **138**, 595–598.

OGILVIE H. (1948) Large-intestine colic due to sympathetic deprivation. *Br. Med. J.* **2**, 671–673.

RACK F. J. and CLEMENT K. W. (1954) Cecostomy and colostomy in acute colon obstructions. *JAMA* **154**, 307–309.

RAGINS H., SHINYA H. and WOLFF W. I. (1974) The explosive potential of colonic gas during colonoscopic electrosurgical polypectomy. *Surg. Gynecol. Obstet.* **138**, 554–556.

ROBERTSON J. A., EDDY W. A. and VOSSELER A. J. (1958) Spontaneous perforation of the cecum without mechanical obstruction. *Am. J. Surg.* **96**, 448–452.

TURNBULL R. E., HAWK W. A. and WEAKLEY F. L. (1971) Surgical treatment of toxic megacolon: ileostomy and colostomy to prepare patients for colectomy. *Am. J. Surg.* **122**, 325–330.

WANEBO H., MATHEWSON C. and CONOLLY B. (1971) Pseudo-obstruction of the colon. *Surg. Gynecol. Obstet.* **133**, 44–48.

WANGENSTEEN O. H. (1955) *Intestinal Obstructions*, 3rd ed. Oxford, Blackwell, p. 838.

WOJTALIK R. S., LINDENAUER S. M. and KAHN S. S. (1973) Perforation of the colon associated with adynamic ileus. *Am. J. Surg.* **125**, 601–606.

YEO R. (1967) Spontaneous perforation of the cecum: case reports and a review of the literature. *Postgrad. Med. J.* **43**, 65–67.

Br. J. Surg. Vol. 62 (1975) 387–393

Epidermoid cysts, polyposis coli and Gardner's syndrome

BARBARA LEPPARD AND H. J. R. BUSSEY*

SUMMARY

One hundred and ninety-six members of 15 families with Gardner's syndrome were investigated to determine the type of skin cyst that is part of this syndrome. These were shown to be epidermoid cysts and not pilar cysts or steatocystoma multiplex. They were solitary or multiple and seldom large and disfiguring. The skin cysts often occurred before the intestinal polyps were detectable. The presence of epidermoid cysts in children should be an indication for sigmoidoscopy when the child reaches the age of 14 years, and at 3-yearly intervals thereafter up to the age of 30 years, whether or not there is a family history of polyposis coli.

At present it is not possible to say if Gardner's syndrome is the same as, or different from, familial polyposis. Until all patients with colonic polyps have a full clinical examination, looking for skin cysts and osteomas, X-rays of the skull and long bones to detect osteomas and dental X-rays for abnormalities of the teeth this question will remain unanswered.

FAMILIAL polyposis coli is an inherited condition in which many hundreds or even thousands of adenomatous polyps develop in the colon and rectum. It frequently manifests itself at an early age (20–30 years) and is associated with a high incidence of intestinal carcinoma. The familial nature of the disease was first noted by Cripps (1882), and its inheritance as a Mendelian autosomal dominant trait was established by 1930 (Dukes, 1930).

During the years 1950–3, Gardner and his co-workers (Gardner and Stephens, 1950; Gardner, 1951; Gardner and Plenk, 1952; Gardner and Richards, 1953) published a series of papers describing a family in which several members were affected with a triad of lesions, that is, (1) multiple adenomatous polyposis of the large intestine, (2) multiple osteomas of the skull and mandible and (3) multiple epidermoid cysts and fibromas of the skin. This syndrome, later named after Gardner, has been extended by the addition of other features such as dental abnormalities, desmoid tumours of the abdominal wall and abdomen and malignant disease of the thyroid gland and periampullary region of the duodenum. Some of these extracolonic lesions may be present for a long time before the intestinal polyps give rise to symptoms. Apart from the large bowel adenomas which are always present, the most constant component of Gardner's syndrome on clinical examination is the occurrence of epidermoid cysts.

An investigation into the nature, incidence and mode of inheritance of the skin cysts of Gardner's syndrome was carried out as part of a large survey of benign familial skin tumours.

Present study

Ascertainment

The St Mark's Hospital Polyposis Register, which was established in 1925 by Dr Cuthbert Dukes, now contains details of 200 families with at least one member affected with polyposis coli. One hundred and ninety-six members of 15 of these families were investigated. Some individuals were seen in the outpatients' department or in the wards of St Mark's Hospital and others were visited in their homes. Letters were sent to those who lived too far away to be visited, and hospital notes and histopathological specimens were obtained when possible and, in particular, for any patient who had died before the study began. Sixty patients were seen and examined by one of us (B. L.) either at the hospital or at home. Information from hospital notes was available on 82 patients, 25 replied to letters and information on the other 29 was obtained from other members of their families.

Method of investigation

When the patients were first seen pedigree details were recorded, a full medical history was taken and a complete clinical examination was carried out. If the patient was over 14 years of age sigmoidoscopy and biopsy of rectal polyps, if these were present, were done and the extent of the polyposis delineated by barium enema examination. When a patient was discovered to have polyposis coli, as many of his relatives as possible were then seen and examined.

Results

Intestinal polyps

Of the 196 patients for whom information was available, there were 108 who were likely to be affected and 88 who were definitely unaffected. Of the 108 possibly affected individuals, 74 definitely had polyposis coli, 5 died of carcinoma of the colon or rectum before the age of 40 years and therefore were probably affected, 5 aged between 20 and 30 years had no polyps on sigmoidoscopy and were probably unaffected and 24 under the age of 17 years either showed no polyps on sigmoidoscopy or were too young to have been examined by sigmoidoscopy. The rest of this paper will be confined to a discussion of the 74 definitely affected patients.

---

* St Mark's Hospital, London.
Present address of B. Leppard: St John's Hospital for Diseases of the Skin, London WC2H 7BJ.

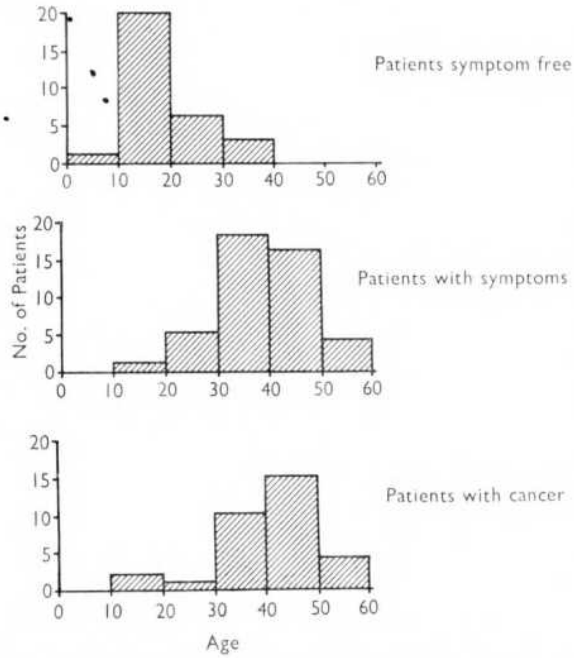


Fig. 1. Age at which polyps were discovered in 74 affected individuals from 15 families.

Approximately half of the affected patients (38 cases) had complained of intestinal symptoms such as rectal bleeding, diarrhoea, constipation or abdominal pain. The age of onset of the symptoms varied between 17 and 60 years, with a mean of 40 years. Polyposis was discovered in the other 36 individuals when they were examined because of a positive family history. The age at which the polyps were found in this group varied from 10 to 57 years of age, with an average of 23 years. This difference between the two groups was statistically significant ($P < 0{\cdot}05$ using the *t*-test). Thirty-nine patients were found to have a carcinoma when their colons were removed. From *Fig.* 1 it can be seen that the age of discovery of polyps for those in whom a carcinoma was found at colectomy was very similar to that of those with bowel symptoms, which suggested that the age of onset of symptoms probably corresponded to the age at which malignant change took place in one or more of the polyps.

Skin cysts

Incidence and type of cyst in polyposis patients: Cysts of the skin were found in 39 (53 per cent) of the 74 patients with polyposis. Microscopical examination of 24 cysts from 15 patients all showed the characteristic features of epidermoid cysts (*Fig.* 2*a*). No

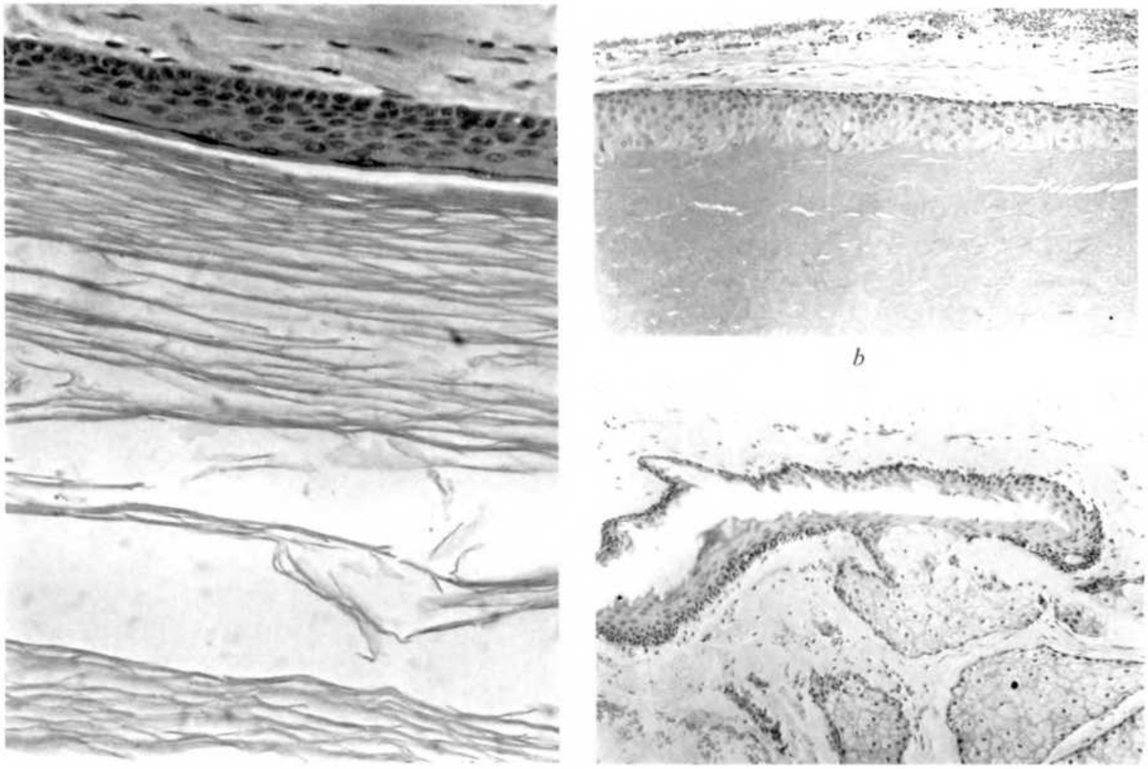

a *b* *c*

Fig. 2. Histological features of 'sebaceous cysts'. *a*, Epidermoid cyst. The lining is the same as normal epidermis, with a gradual flattening of cells as they mature, a granular layer and flaky basophilic-staining keratin in the centre. HE. (× 96.) *b*, Pilar cyst. Individual cells become bigger and fatter as they mature and the centre of the cyst is filled with solid eosinophilic-staining keratin. HE. (× 72.) *c*, Steatocystoma multiplex. The lining cells are different from both (*a*) and (*b*). Individual cells break off into the centre of the cyst and sebaceous glands are seen to make up part of the cyst wall. HE. (× 72.)

examples of pilar cysts or steatocystoma multiplex were found.

Number and position of cysts: The number of cysts per patient varied from 1 to 20, the average being 4. Thirteen (33 per cent) of the 39 patients had solitary cysts. Of those with multiple cysts, in only 1 patient were they large and disfiguring. The site of the cysts is shown in *Fig.* 3. The commonest site was the legs, followed by the face, scalp and arms. The trunk was relatively seldom involved.

Age distribution: The age of onset of the cysts was from birth to 35 years, with an average of 13 years. This was statistically significantly earlier than the clinical manifestations of the colonic polyps ($P < 0{\cdot}01$) and confirms previous observations that the cysts might be used as a guide to indicate which members of a family would later develop polyps (Gardner and Richards, 1953; Coli et al., 1970).

In a group of patients with epidermoid cysts, but without Gardner's syndrome, the average age of onset of these cysts was found to be 26 years, with a range from birth to 58 years (Leppard, 1975). Only 2 patients in this group were found to have cysts before the age of 15 years. On the other hand, 13 (18 per cent) of the 74 patients in this study who had polyposis coli had cysts removed in childhood without the diagnosis of Gardner's syndrome being considered.

Table I: ASSOCIATED LESIONS OF GARDNER'S SYNDROME IN 74 PATIENTS

Lesion	Affected individuals	
	No.	%
Epidermoid cysts	39	53
Osteomas	18	24
Abnormal dentition	13	18
Desmoid tumours	5	7
Malignant tumours (other than those of the rectum and colon)	5	7

Association with other lesions of Gardner's syndrome: Details of the 74 polyposis patients who had the various lesions of Gardner's syndrome are given in *Table I.*

Clinical features

The affected individuals in 4 pedigrees will be described (*Fig.* 4). These pedigrees illustrate the chief points seen in the 15 families investigated.

Pedigree A

II.2: I. S., male, aged 43 years. The proband first developed a cyst on the back of his neck at the age of 26 years and a second on his forehead at the age of 30. Four years later he had an osteoma removed from his right great toe. At the age of 37 years he developed diarrhoea and rectal bleeding and was found to have polyposis coli and a carcinoma arising from the largest of the polyps. He was treated by panproctocolectomy and ileostomy.

III.1: G. S., female, aged 20 years. She first developed a cyst on the forehead at the age of 8 years and since then 4 more have appeared on the right temple, left cheek, right calf and over the

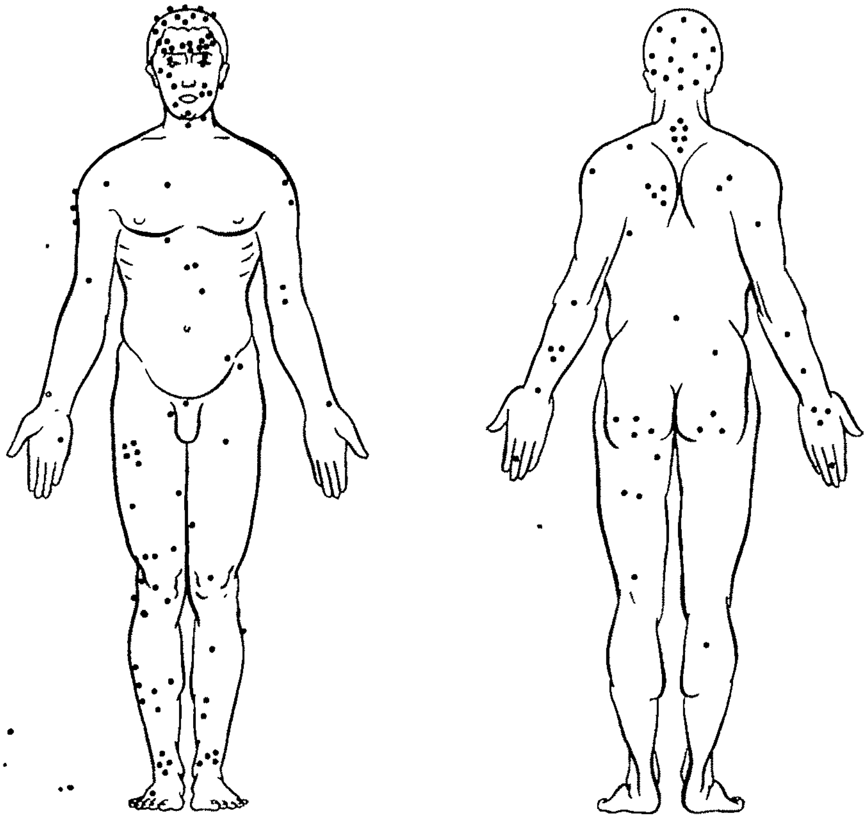


Fig. 3. Site of cysts.

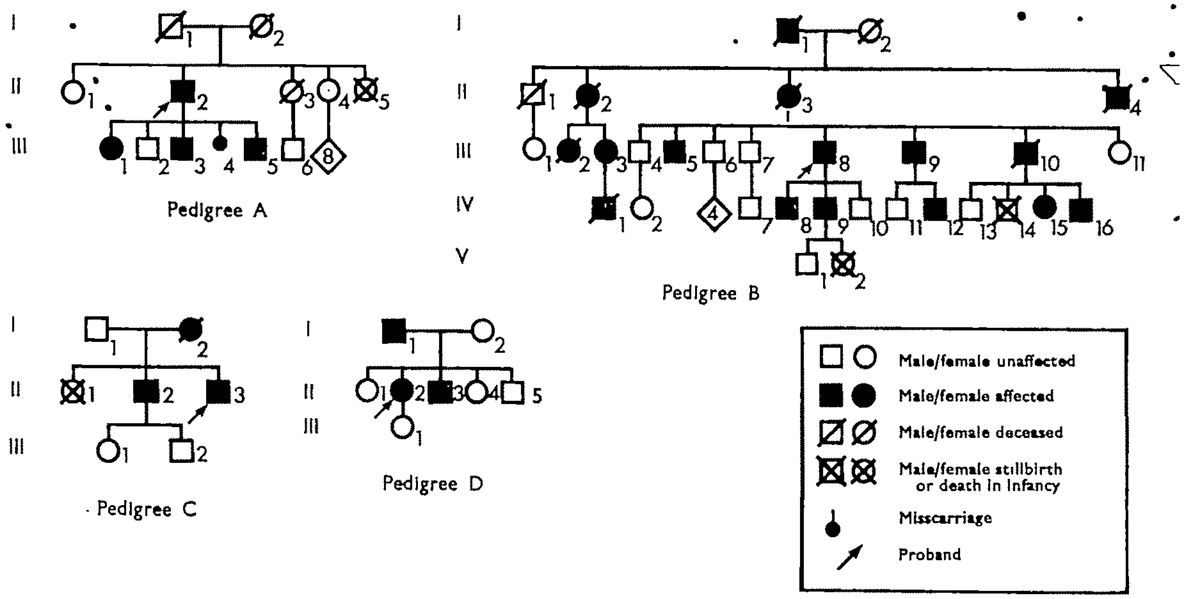


Fig. 4. The 4 pedigrees studied in detail.

right deltoid respectively. Because her father was known to have polyposis coli she was examined by sigmoidoscopy at the age of 13 years and found to have a few polyps. At the age of 17 years she developed rectal bleeding; a colectomy and ileorectal anastomosis were performed a year later. She had no obvious osteomas but she had 2 unerupted teeth in the left upper jaw.

III.2: P. S., male, aged 18 years. He had no cysts on the skin, no obvious osteomas or abnormalities of his teeth and sigmoidoscopy on four occasions was normal. He is regarded at present as unaffected.

III.3: P. S., male, aged 16 years. He first developed a cyst on the scalp at the age of 18 months and a second one on his right ankle at the age of 10 years. Sigmoidoscopy at the age of 13 years showed a few polyps in the rectum and a biopsy of one of them was reported as an adenomatous polyp. He had no osteomas or abnormalities of his teeth.

III.5: M. S., male, aged 14 years. He had 2 cysts, 1 on the left side of his back and 1 on the right thigh, which had been present since early childhood. Sigmoidoscopy in 1974 confirmed that he also had polyposis.

Comment: In this family all the individuals with polyposis coli have skin cysts, in contrast to pedigrees B, C and D.

Pedigree B

III.8: G. P., male, aged 61 years. The proband began to develop cysts at the age of 16 years and has had 4 altogether, 2 on his face, 1 on the left arm and 1 on the right shin. At the age of 18 years he noticed a hard bony lump at the left angle of his jaw and since then 2 other osteomas have appeared on the left side of his scalp. At the age of 41 years he was admitted as an emergency to another hospital where he was found to have polyposis coli and a carcinoma at the rectosigmoid junction. He was transferred to St Mark's Hospital where colectomy and ileorectal anastomosis were performed.

I.1: M. K., male. He died aged 48 years of a carcinoma of the bowel.

II.2: E. D., female. She died aged 49 years of a carcinoma of the bowel.

II.3: E. P., female. She died aged 49 years of a carcinoma of the colon. Several members of the third generation remember her as having a large cyst on the scalp.

II.4: S. K., male. He died aged 49 years of a carcinoma of the colon.

III.2: M. W., female. At the age of 45 years she developed colicky abdominal pain and irregular diarrhoea. Sigmoidoscopy showed multiple polyps in the rectum. A colectomy and ileorectal anastomosis were performed. All the lesions were benign, but she died of a pulmonary embolus 3 days postoperatively.

III.3: H. de L., female, aged 55 years. At the age of 29 years she developed rectal bleeding. Sigmoidoscopy showed large numbers of polyps in the rectum. A colectomy and ileorectal anastomosis were performed and she has remained well since then. She lives in Canada, but in a recent letter she said that she had never had any cysts on the skin or obvious bony lumps.

III.5: J. P., male. At the age of 32 years he was investigated for chronic diarrhoea and found on barium enema examination to have a mass in the midsigmoid region. Laparotomy revealed a carcinoma with malignant glands along the aorta. He died a few months later.

III.9: G. P., male, aged 59 years. He first noticed cysts on the skin at the age of 12 years and he has had 10 on his face, scalp and legs. He was first seen at St Mark's Hospital when aged 38 years because his brother (III.8) had been found to have polyposis. G. P. was also found to have polyps and a colectomy and ileorectal anastomosis were performed. At the age of 57 years he had all his teeth removed because of dental caries, at which time the dentist noticed an osteoma of the mandible.

III.10: V. P., male, aged 53 years. This patient had 8 cysts on the skin which first appeared at the age of 21 years. In his mid-twenties he developed diarrhoea and rectal bleeding and at the age of 29 years he was found to have a carcinoma of the rectum. An abdominoperineal excision of the rectum was performed, leaving the patient with a colostomy. At the age of 46 years he had an episode of subacute intestinal obstruction and rapidly lost 6·4 kg in weight. Investigation showed him to have polyposis coli and two separate carcinomas of the colon. A total colectomy and ileostomy were performed. Three years later he became jaundiced and was found to have a carcinoma of the ampulla of Vater which was removed by pancreaticoduodenectomy. At operation there were several small duodenal polyps which were reported as hamartomas on histological examination. Three years after this third operation he developed widespread metastases and died.

IV.1: D. McL., male. Routine sigmoidoscopy at the age of 15 years showed that this patient had polyps in the rectum. At the age of 17 years he developed raised intracranial pressure and at operation was found to have a medulloblastoma. He died 3 days postoperatively.

IV.8: R. P., male, aged 28 years. He was mentally retarded. Polyposis was discovered by routine sigmoidoscopy at the age of 17 years. He had 1 cyst on his right buttock which appeared at the age of 23 years. He had no osteomas, but at the age of 28 years he still had all his first dentition.

IV.9: C. P., male, aged 26 years. At the age of 15 years he was found to have polyps on sigmoidoscopic examination. He had 1 cyst on his right forearm and 2 osteomas, 1 on the left maxilla and 1 on the scalp.

IV.12: B. P., male, aged 27 years. He developed cysts on the skin, a large lipoma on the back of his neck and an osteoma of the left mandible at the age of 11 years. Polyposis was found at the age of 12 years by sigmoidoscopy.

IV.15: C. S., female, aged 27 years. She first developed an osteoma on the back of the scalp at the age of 11 years, and now has 2 in the occipital region and 1 on her right middle finger. Polyposis was discovered at the age of 19 years and colectomy and ileorectal anastomosis were carried out a year later. Fourteen months after colectomy she developed a large mass in the abdomen and at laparotomy was found to have several desmoids in the mesentery of the small bowel. Because of their large size it was impossible to remove them. She has never had any cysts on the skin.

IV.16: C. P., male, aged 20 years. Polyposis was found at the age of 12 years by sigmoidoscopy. He had no cysts or osteomas visible and no obvious abnormality of his teeth.

Comment: In this family only about half of the affected members had skin cysts. Approximately half also had osteomas, but desmoid tumours were seen in 1 patient (IV.15) and abnormalities of the teeth were only present in 1 patient (IV.8). Two patients had tumours of other organs—a medulloblastoma in IV.1 and a carcinoma of the ampulla of Vater in III.10. One patient (IV.16) had no features of Gardner's syndrome other than the polyposis coli. Some details of this family were first reported by Parks et al. (1970).

Pedigree C

In this family none of the affected members had cysts. The mother (I.2) died at the age of 54 years with a carcinoma of the rectum and polyposis coli. Both her sons (II.2 and II.3) had osteomas. The proband (II.3) had an osteoma of the left mandible which became clinically obvious at the age of 13 years and interfered with his performance on the violin. It was removed surgically and shown histologically to be an osteoma. His brother (II.2) had only 1 small osteoma in the left parietal region, but he has had a Sertoli cell tumour of the left testis. Neither brother had cysts of the skin or obvious dental abnormalities; no desmoid tumours have developed in the 13 years since colectomy. The 2 children of II.2, aged 6 and 3 years respectively, as yet show no evidence of cysts or osteomas.

Pedigree D

In this Negro family only the proband (II.2) had any features additional to the polyposis coli. This patient, a 19-year-old female, developed a large desmoid tumour of the mesentery of the small bowel at the age of 16 years. Two years later she had a recurrent desmoid tumour in the abdominal wall and the diagnosis of polyposis coli was considered. Polyps were found on sigmoidoscopy, and colectomy and ileorectal anastomosis were carried out at the age of 19 years. When this was done 2 further desmoid tumours were present in the anterior abdominal wound. She had no cysts or osteomas on clinical examination and her teeth appeared normal.

Genetic findings

From the 4 pedigrees shown in *Fig.* 4 it can be seen that polyposis coli is inherited as an autosomal dominant trait. Taking all the 15 families and excluding the probands and the affected individuals in the older generations for whom there is only hearsay evidence, we saw 56 affected patients (27 males and 29 females) and 70 unaffected individuals (36 males and 34 females). This gives an approximation to a 1 : 1 ratio both in total numbers of affected to unaffected and in numbers of males to females. All the affected individuals had the intestinal polyps, but the other lesions of Gardner's syndrome were present in varying combinations in different families and in different members of the same family. This was very apparent in pedigree B.

Discussion

Skin cysts in Gardner's syndrome have been referred to as 'sebaceous cysts', 'epidermoid inclusion cysts', 'sebocystomatosis' (steatocystoma multiplex) and 'atheromas'. These terms seem to have been used interchangeably, as if they represented the same condition. However, the 'sebaceous cyst' is not a single entity but any one of three conditions—pilar cysts, epidermoid cysts or steatocystoma multiplex.

Pilar cysts, the common wens, present as solitary or multiple firm intradermal or subcutaneous swellings, usually on the scalp. They have no obvious punctum. Epidermoid cysts may be solitary or multiple, they occur anywhere on the body surface and frequently, but not always, have a visible punctum. Clinically, pilar cysts and epidermoid cysts may be confused, but the site and the presence or absence of a punctum help to differentiate them. Steatocystoma multiplex presents a different clinical picture. Individual lesions are small (0·5–0·8 cm), skin-coloured or yellow or bluish intradermal nodules, which are always multiple. They are situated on the front of the chest or in the axillae and groins. They appear in the late teens or early twenties and then remain static for the rest of the patient's life. Histological examination of the three types of cyst shows them to be quite distinct (*Fig.* 2).

The cysts we found in Gardner's syndrome were epidermoid cysts and not pilar cysts or steatocystoma multiplex. They were either solitary or multiple and most patients had only a small number. Although they could be disfiguring, as they were in one of our patients and in many of the reports in the literature (e.g. Weary et al., 1964), they were often small and not noticed by the patient. In none of our families were they obvious as a family trait. This is in contrast to most of the reports of Gardner's syndrome, which stress very numerous large cysts (Oldfield, 1954; Fader et al., 1962).

The skin cysts can be seen many years before the intestinal polyps, but they do not necessarily occur in all the affected members of a family (contrast pedigrees A and B). Although they may be a guide as to which individuals will later develop polyps, this is not entirely reliable. However, all the patients who had cysts also had, or later developed, polyps.

Eighteen per cent of the patients in this study had cysts removed in childhood without the diagnosis of Gardner's syndrome being considered. This is the usual pattern of events, the diagnosis only being considered when bowel symptoms develop (Duncan et al., 1968). This is shown very well by the three reports of a family from Leeds. In 1937 Ingram and Oldfield first reported this family as having hereditary sebaceous cysts. These were called 'steatocystoma multiplex', but from the clinical description and histological features they were epidermoid cysts. Two brothers and a sister were described who had numerous, large and disfiguring cysts on the face, scalp, trunk and limbs in childhood. Seventeen years later Oldfield (1954) reported the same family, having found, when bowel symptoms developed, that its members had polyposis coli. Two of these patients died (at the age of 32 and 31 years) with carcinoma of the rectosigmoid and rectum respectively. In 1970 one member of the same family was included in a study by McAdam and Goligher (*Case* 3) because, in addition to the cysts and polyposis coli, he developed multiple desmoid tumours. This family therefore, probably fits best into the diagnosis of Gardner's syndrome.

Epidermoid cysts are very uncommon in children (Leppard, 1975), and those who develop them before puberty should probably have a sigmoidoscopic examination every 3 years from the age of 14 years onwards, whether or not there is a family history of polyposis coli. Individuals of any age who present with pilar cysts or steatocystoma multiplex do not need routine sigmoidoscopy.

There is considerable difficulty in defining Gardner's syndrome. The original description by Gardner (1951) included patients with polyposis coli and multiple hard and soft tissue tumours. In 1962 and 1969 he modified this somewhat to include dental abnormalities as well. Thomas et al. (1968) accepted patients with the original triad of lesions with or without a positive family history or a patient with one or more of these manifestations in whose family there were members with the complete triad. Possibly the term should be applied to families rather than individuals. The mode of inheritance as an autosomal dominant trait is not in dispute, but whether one or several genes are involved is unknown. McKusick (1962) believed that Gardner's syndrome is determined by a single gene which is distinct from that for polyposis coli alone. On the other hand, Smith (1968) believed that Gardner's syndrome is the complete manifestation of a spectrum of pathological changes which could affect in variable numbers and combinations any patient who had multiple polyposis. He maintained that patients with polyposis coli who have these extra features do not form a special subgroup and that one gene mutation only is necessary to explain all the lesions.

Families C and D include individuals diagnosed as suffering from familial polyposis, some of whom also had additional lesions. Two brothers in family C had osteomas and 1 member of family D had desmoid tumours. None of these patients had epidermoid cysts and no member of these 2 families had the complete triad. The more intensive the search for extracolonic lesions in patients with polyposis coli, the greater the number found to be present. Only when all such patients have a full clinical examination for surface tumours, X-rays of the skull and long bones to detect osteomas and X-rays of the jaws to exclude dental abnormalities will it be possible to determine the incidence of the various lesions. It is possible that such complete investigations will increase the incidence rate of extracolonic lesions associated with polyposis coli but will not alter the variable expression of these lesions recorded so far. They should, however, resolve the problem of whether or not familial polyposis and Gardner's syndrome are genetically different diseases.

Acknowledgements

We thank the consultant surgeons at St Mark's Hospital for their permission to examine and visit their patients, Dr B. Morson for help with the histological studies and Dr R. S. Wells for his help in the preparation of this manuscript.

References

COLI R. D., MOORE J. P., LA MARCHE P. H., DE LUCA F. G. and THAYER W. R. (1970) Gardner's syndrome. A revisit to a previously reported family. *Am. J. Dig. Dis.* **15**, 551–568.

CRIPPS W. H. (1882) Two cases of disseminated polyps of rectum. *Trans. Path. Soc. Lond.* **33**, 165–168.

DUKES C. (1930) The hereditary factor in polyposis intestini, or multiple adenomata. *Cancer Rev.* **5**, 241–256.

DUNCAN B. R., DOHNER V. A. and PRIEST J. H. (1968) The Gardner syndrome: need for early diagnosis. *J. Pediatr.* **72**, 497–505.

FADER M., KLINE S. N., SPATZ S. S. and ZUBROW H. J. (1962) Gardner's syndrome (intestinal polyposis, osteomas, sebaceous cysts) and a new dental discovery. *Oral Surg.* **15**, 153–172.

GARDNER E. J. (1951) A genetic and clinical study of intestinal polyposis, a predisposing factor for carcinoma of the colon and rectum. *Am. J. Hum. Genet.* **3**, 167–176.

GARDNER E. J. (1962) Follow up study of a family group exhibiting dominant inheritance for a syndrome including intestinal polyps, osteomas, fibromas and epidermal cysts. *Am. J. Hum. Genet.* **14**, 376–390.

GARDNER E. J. (1969) Gardner's syndrome re-evaluated after twenty years. *Proc. Utah Acad. Sci.* **46**, 1–11.

GARDNER E. J. and PLENK H. P. (1952) Hereditary pattern for multiple osteomas in a family group. *Am. J. Hum. Genet.* **4**, 31–36.

GARDNER E. J. and RICHARDS R. C. (1953) Multiple cutaneous and subcutaneous lesions occurring simultaneously with hereditary polyposis and osteomatosis. *Am. J. Hum. Genet.* **5**, 139–147.

GARDNER E. J. and STEPHENS F. E. (1950) Cancer of the lower digestive tract in one family group. *Am. J. Hum. Genet.* **2**, 41–48.

INGRAM J. T. and OLDFIELD M. C. (1937) Hereditary sebaceous cysts. *Br. Med. J.* **1**, 960–962.

LEPPARD B. (1975) In preparation.

MCADAM W. A. F. and GOLIGHER J. C. (1970) The occurrence of desmoids in patients with familial polyposis coli. *Br. J. Surg.* **57**, 618–631.

MCKUSICK V. A. (1962) Genetic factors in intestinal polyposis. *JAMA* **182**, 271–277.

OLDFIELD M. C. (1954) The association of familial polyposis of the colon with multiple sebaceous cysts. *Br. J. Surg.* **41**, 534–541.

PARKS T. G., BUSSEY H. J. R. and LOCKHART-MUMMERY H. G. (1970) Familial polyposis coli associated with extracolonic abnormalities. *Gut* **11**, 323–329.

SMITH W. G. (1968) Familial multiple polyposis: research tool for investigating the etiology of carcinoma of the colon? *Dis. Colon Rectum* **11**, 17–31.

THOMAS K. E., WATNE A. L., JOHNSON J. G., ROTH E. and ZIMMERMANN B. (1968) Natural history of Gardner's syndrome. *Am. J. Surg.* **115**, 218–226.

WEARY P. E., LINTHICUM A., CAWLEY E. P., COLEMAN C. C. jun. and GRAHAM G. F. (1964) Gardner's syndrome. *Arch. Dermatol.* **90**, 20–30.

Br. J. Surg. Vol. 62 (1975) 394–396

Chronic hydradenitis suppurativa: a report of 9 cases

HUMPHREY PIGOTT AND HAROLD ELLIS*

SUMMARY

This paper describes the treatment of 9 patients suffering from hydradenitis suppurativa all of whom were treated by surgical excision. The aetiology, diagnosis and treatment by surgical excision are discussed.

HYDRADENITIS suppurativa is an ill-recognized chronic inflammation of the apocrine glands of the skin. These glands differ in structure, function and distribution from the more numerous tubular eccrine sweat glands and compound areolar sebaceous glands. Failure to diagnose this chronic disabling condition often results in delay of effective treatment.

This paper describes 9 patients suffering from the condition, 8 of whom were initially incorrectly diagnosed with subsequent delay in reaching surgical cure.

Case reports

Case 1: S. S., a hairdresser aged 22 years, complained of persistent discharging axillary sinuses from the age of 19, for which she had been treated with repeated unsuccessful courses of antibiotics and local radiotherapy. On examination there was active hydradenitis suppurativa in the right axilla. In November 1969 local excision with primary suture was performed, with no subsequent abscess formation.

Case 2: C. T., an ex-SRN aged 39 years, had suffered from persistent discharging axillary sinuses of the left axilla for 3 years, and had been treated with repeated unsuccessful courses of antibiotics. On examination active hydradenitis suppurativa was present. Culture of the pus showed coagulase negative staphylococci. In November 1970 local excision with primary suture of the left axilla was performed. Wound infection delayed healing for 2 months. In September 1971 the patient was readmitted at her own request for excision of active hydradenitis suppurativa of the other axilla. The wound healed well, and no further suppuration of either axilla has occurred.

Case 3: S. L., a pupil nurse aged 19 years, had had discharging abscesses in the axillary skin on both sides from the age of 11. On examination chronic hydradenitis suppurativa was present. In June 1972 the left axillary skin was excised, and in September 1972 the right axillary skin was excised. In January 1973, August 1973 and March 1974 further bilateral excisions of small recurrent sinuses were performed. Typical hydradenitis suppurativa was seen on microscopic examination.

Case 4: K. O'C., a housewife aged 39 years, had had chronic axillary sinuses for 1 year. In November 1973 bilateral axillary skin excision with primary suture was performed. She remains well.

Case 5: S. A., a housewife aged 24 years, had had chronic axillary sinuses for 4 years. Unsuccessful repeated antibiotic courses had been given. On examination typical chronic hydradenitis suppurativa was present (*Fig.* 1). In July 1974 bilateral excision of the axillary skin was performed.

Case 6: M. M., a cleaner aged 44 years, had suffered from severe acne as an adolescent, with recurrent discharging sinuses of the axillae from the age of 18, for which she had received multiple incision and drainage procedures. In 1965 excision of the axillary skin on the right side was performed with split-skin grafting of the skin defect. A similar procedure was performed on the left side in 1967. No further abscesses occurred in either axilla. In January 1973 a persistent discharge from the right groin developed which was treated with local excision and primary suture in February 1974. A recurrent area of hydradenitis suppurativa was excised in May 1974.

Case 7: P. R., a housewife aged 26 years, presented with a 1-year history of intermittent discharging sinuses of both groins, but no axillary symptoms. In June 1972 local excision of the groin skin was performed with primary skin suture. Low grade wound infection delayed healing for 6 weeks. No subsequent sinus formation has occurred. Hydradenitis suppurativa was confirmed on microscopic examination.

Case 8: D. W., a lorry driver aged 50 years, was first seen in 1971 with a 2-month history of inguinoscrotal abscess formation. The initial diagnosis was of an anterior pilonidal sinus, and was treated by incision and drainage. He admitted to frequent recurrent axillary boils for many years. From 1971 to 1972 there was persistent perianal sinus discharge. On examination indurated sinus formation was found at the base of the scrotum. In May 1972 local excision and primary suture was performed with no subsequent sinus formation.

Case 9: J. B., a housewife aged 38 years, was referred to the Surgical Outpatients' Department by the Westminster Hospital Casualty Department with a diagnosis of hydradenitis suppurativa (*Fig.* 2). The disease had been present for 1 month, localized to the right axilla. She was treated by excision and primary suture in August 1974.

Discussion

The first description of hydradenitis suppurativa is attributed by Conway et al. (1952) to Velpeau in 1839. The existence of the apocrine glands was shown by Robin in 1845. These glands are gathered into small groups and discharge into the cavity of the hair sheath (*Fig.* 3). They represent a scent gland of sexual function in certain lower animals and are influenced by the endocrine changes of the menstrual cycle. Greeley (1951) suggested that a similar pubertal activation of the glands occurs in man, where they are found in the axilla, areola of the breast, subumbilical and inguinal areas, as well as in the perianal region, where they are known as the glands of Gay (Williams, 1953). Hydradenitis suppurativa only occurs in the areas where there are apocrine glands.

Most of the reports of hydradenitis suppurativa emphasize the delay in reaching the diagnosis (Conway et al., 1952). This feature is supported by all our cases except one (*Case* 9). Most of our patients had received repeated courses of systemic antibiotics, local applications and the use of bactericidal soaps without benefit. Brunsting (1939) mentioned how the diagnosis is often obscured under many miscellaneous names such as abscess, furunculosis, pyoderma, chronic undermining burrowing ulcer of the skin and non-specific granuloma. The chronic nature of the disease with extensive

---

* Surgical Unit, Westminster Medical School, London.

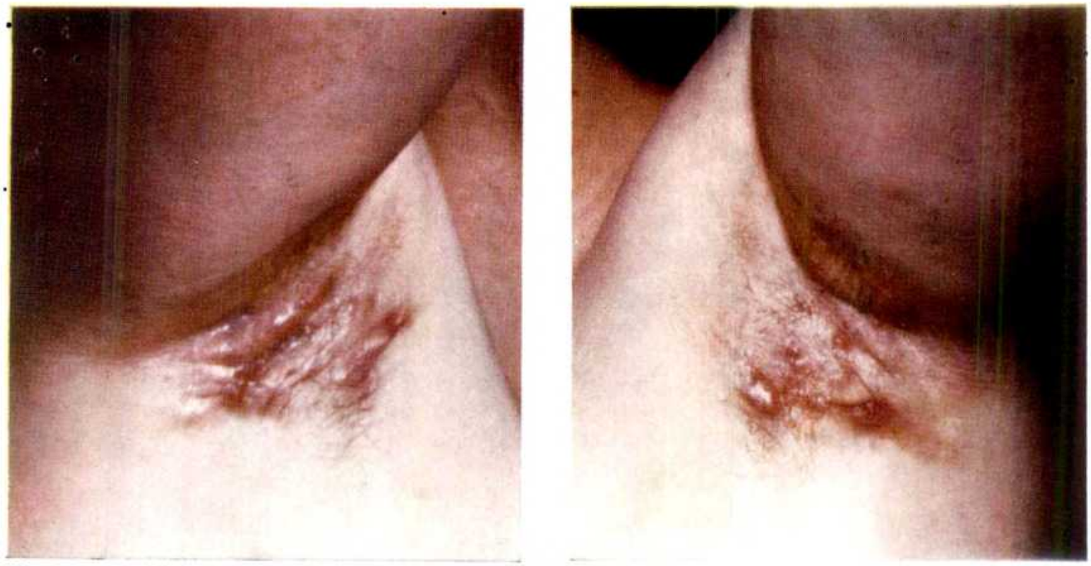


Fig. 1. *Case* 5. Clinical photograph of active hydradenitis in the axilla.

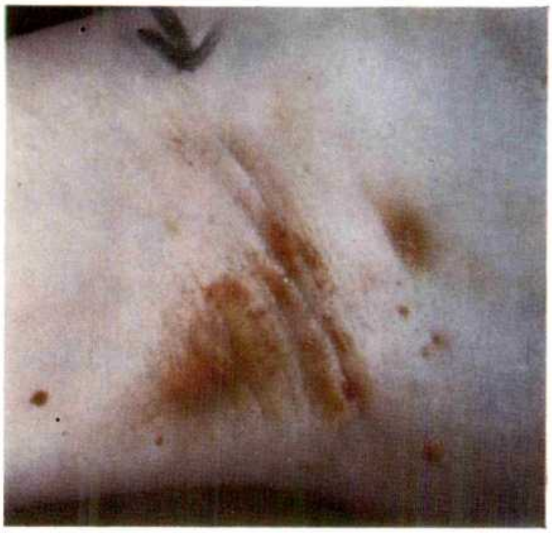


Fig. 2. *Case* 9. Clinical photograph of the right axilla.

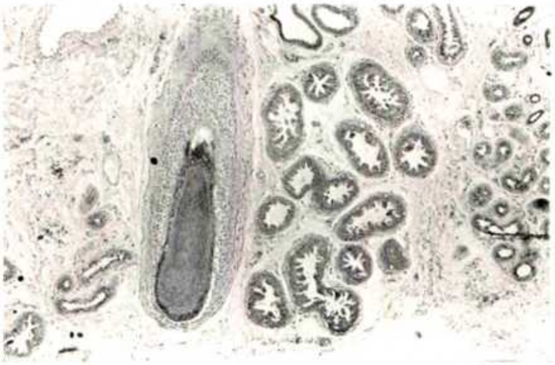


Fig. 3. Photomicrograph of a normal apocrine gland showing the adjacent hair follicle. (× 50.)

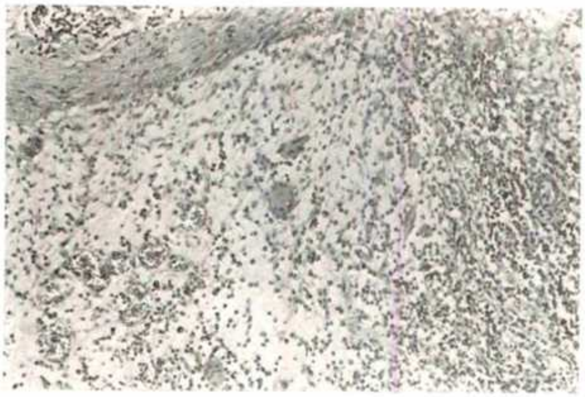


Fig. 4. Photomicrograph of active hydradenitis suppurativa showing granulation tissue and the characteristic 'Langhans-type' giant cells. (× 75.)

and persistent sinuses in the subcuticular fat layer is, however, characteristic, and, once recognized, easy enough to diagnose almost at a glance.

Williams (1953) has drawn attention to the scarcity of reports in the English journals, but the account of 388 patients collected over an 8-year period at the Mayo Clinic suggests that the disease may be more common than is appreciated (Jackman and McQuarrie, 1949). The condition is most often found in the third and fourth decades of life (Masson, 1969). The sex incidence appears to be equal for the common axillary lesion, but men are more liable to the perianal disease.

The initial lesion is a superficial abscess which progresses to the characteristic chronic indolent inflammatory disease of the skin with indurated scar tissue burrowing into the subcutaneous fat. Microscopic examination shows the initial infection to be confined to the apocrine glands, with subsequent involvement of the adjacent eccrine glands. The infection spreads through the subcutis via distended lymphatic channels.

In the florid case there is extensive local destruction with chronic inflammatory cells and dense fibrous tissue formation (*Fig.* 4). Large pale-staining giant cells can be seen, which may represent the remnants of the epithelial cells which line the apocrine gland (Brunsting, 1939).

Bacteriological culture usually shows a coagulase positive or negative staphylococcal infection. In long standing cases the variety of bacteria is greater (Masson, 1969).

Surgery offers the only chance of control of the well-established condition, athough it may have to be repeated several times to remove local recrudescences, as shown by *Case* 3. Chronic hydradenitis suppurativa cannot effectively be treated by systemic or local antibiotics and bactericidal solutions are equally inappropriate.

Excision with primary suture is simple and effective for small areas such as the axilla (*Case* 5). This method is also suitable for the groin, as is demonstrated by *Case* 7, although recurrent areas may require re-excision. The chronic inflammatory nature of the condition leads to occasional wound breakdown following primary suture, but this can be minimized with the application of local antibiotic powder such as ampicillin 1 g prior to wound closure. Large areas of axillary skin excision may give rise to unsightly contractures which can be avoided by split-skin grafting or rotational skin flaps (Harrison, 1964). Primary suture with Z-plasty has been advocated for such axillary excisions (Greeley, 1950).

Perianal hydradenitis occurs more commonly in men. *Case* 8 illustrated the frequent occurrence of the condition in lorry drivers which has been previously described (Adams and Harsten, 1972). Small areas can be treated by excision and suture, but when larger areas are found, more extensive excision with skin grafting may be required and preceded by faecal diversion via a colostomy (Ching and Stahlgreen, 1965). It is in these extensive perianal suppuration problems that the condition may be confused with Crohn's disease.

Acknowledgements

We greatly appreciate the help given to us by the Department of Photography and Medical Illustration, Westminster Hospital, London.

We should also like to thank Dr Peter E. Nicholls for his advice on the pathology findings.

References

ADAMS J. D. and HARSTEN A. S. (1972) Perianal hydradenitis suppurativa. *Surg. Clin. North Am.* **52**, 467–472.

BRUNSTING H. A. (1939) Hydradenitis suppurativa; abscess of the apocrine sweat glands. *Arch. Dermatol. Syph.* **39**, 108–120.

CHING C. C. and STAHLGREEN L. H. (1965) Clinical review of hydradenitis suppurativa: management of cases with severe perianal involvement. *Dis. Colon Rectum* **8**, 349–352.

CONWAY H., STARK R. B., CLIMO S., WEETER J. C. and GARCIA F. A. (1952) The surgical treatment of chronic hydradenitis suppurativa. *Surg. Gynecol. Obstet.* **95**, 455–464.

GREELEY P. W. (1950) Surgical treatment of chronic suppurative hydradenitis. *Arch. Surg.* **61**, 193–198.

GREELEY P. W. (1951) Plastic surgical treatment of chronic suppurative hydradenitis. *Plast. Reconstr. Surg.* **7**, 143–146.

HARRISON S. H. (1964) Axillary hydradenitis. *Br. J. Plast. Surg.* **17**, 95–98.

JACKMAN R. H. and MCQUARRIE H. B. (1949) Hydradenitis suppurativa. *Am. J. Surg.* **77**, 349–351.

MASSON J. K. (1969) Surgical treatment for hydradenitis suppurativa. *Surg. Clin. North Am.* **49**, 1043–1052.

ROBIN C. (1845) Note sur une espèce particulière de glandes de la peau de l'homme. *Ann. Sci. Nat. Paris*, Troisième Série zoologie, **4**, 380–381.

WILLIAMS D. W. (1953) Surgical treatment of suppurative hydradenitis. *Br. J. Plast. Surg.* **6**, 231–237.

NEW
Praxilene
vasoactivator
INJECTABLE
RELIEVES REST PAIN

NEW

for peripheral vascular disorders

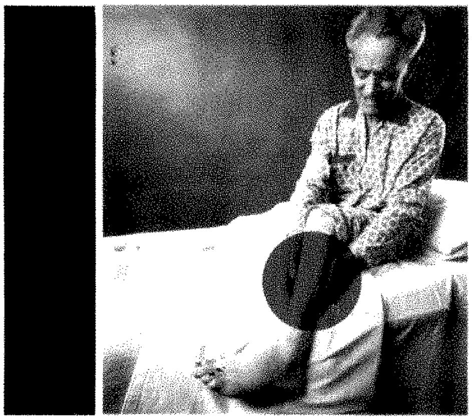
Praxilene

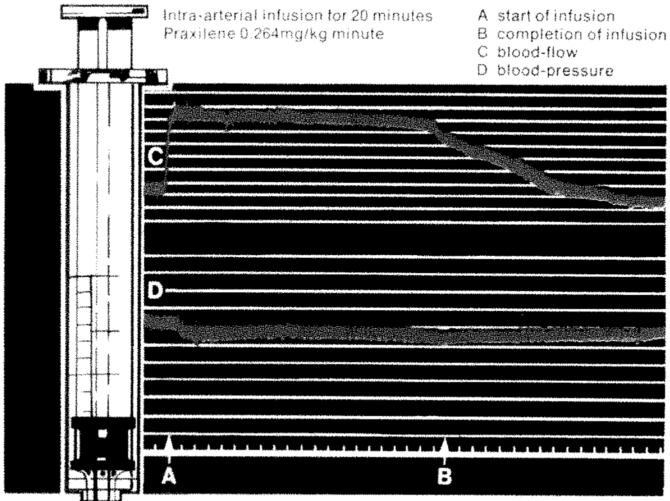
vasoactivator

INJECTABLE

RELIEVES REST PAIN

by flushing out pain producing metabolites
by improving blood-flow – without affecting blood-pressure
by a unique metabolic activity





Fast relief
Praxilene administered parenterally (Intra-arterial; Intravenous; Intramuscular) can give relief of pain within as short a time as one week, in many cases.

Prolonged relief
Relief of pain is prolonged: at the same time the collateral circulation is given the opportunity to develop, resulting in an improved blood supply to the affected limb.

Praxilene has produced excellent results because it has a very wide safety margin and the dosage can be individually tailored to the severity of the disorder.

Praxilene: Unique Vasoactivator

Praxilene: Naftidrofuryl: available as 40mg ampoules and 100mg capsules.

Full prescribing information and dosage schedule on request

Lipha (UK)
West Drayton, Middlesex
Telephone: West Drayton 49331/2

Br. J. Surg. Vol. 62 (1975) 397–400

Bilateral extradural haematomas

M. V. SUBRAHMANIAN, G. B. RAJENDRAPRASAD AND B. DIBBALA RAO[*]

SUMMARY

Eleven cases of bilateral extradural haematomas were encountered in a total of 49 cases of extradural haematoma during a period of 4 years among 1000 consecutive cases of acute head injury. Assault was held responsible for 60 per cent of the total head injuries. Most of the patients were seen late; 8 were already unconscious and 5 had dilated fixed pupils. All 11 patients died, 4 soon after admission. Nine cases were found to have associated brain damage at autopsy. In 2 cases bilateral extradural haematomas with compression of the brain were the only intracranial abnormalities. In 4 cases a clot was missed on conventional exploration.

BILATERAL extradural haematomas are rare. The previously reported cases are tabulated in *Table I.*

Table I: NUMBER OF CASES OF EXTRADURAL HAEMATOMA REPORTED IN THE LITERATURE

Author	No. of cases of extradural haematoma	No. of cases of bilateral extradural haematomas	Period of study (yr)
Hooper (1959)	83	5	11
Cabraal and Weinman (1964)	53	2	2
Dayananda Rao et al. (1967)	31	1	7
Gallagher and Browder (1968)	167	4	25
Jamieson and Yelland (1968)	167	5	10
Jain and Kankandy (1969)	8	2	1½
Kalyanaraman et al. (1970)	51	1	20
Sambasivan and Ramachandran (1973)	32	2	5
Soni (1973)	—	1	—
Present series (1975)	49	11	4

Patients

Among 1000 consecutive cases of acute head injury admitted to the Government General Hospital, Guntur, from February 1970 to January 1974, 49 cases of extradural haematoma were encountered either at surgery or at post-mortem examination. Of these, 11 cases were bilateral.

It is our practice to admit all cases of acute head injury under the care of general surgeons whence they can later be referred to the neurological department if necessary. This may involve avoidable delay in an emergency neurosurgical intervention.

We have analysed these 11 cases of bilateral extradural haematomas regarding their cause, clinical manifestations and radiological features in relation to the operative and autopsy findings.

Cause of head injury

Assault was the main cause of head injury in 7 out of 11 cases. Two patients fell from a moving vehicle, another fell 20 feet from a tree and in one case the nature of the accident was not documented. It is obvious from *Table II* that 60 per cent of the head injuries were the result of assault, which probably accounts for the high incidence of extradural haematoma in this region. Sticks, iron rods and axes were used for assault. In the series reported by Cabraal and Weinman (1964) of 53 cases of extradural haematoma, assault was the main cause in 43·4 per cent.

All our patients were males aged between 12 and 60 years. Nine of them were over 25 years of age. The 2 younger patients (*Cases* 8 and 9) sustained head injuries by falling from moving vehicles.

All the patients were admitted to hospital 4–44 hours after sustaining the injury, and their survival ranged from a few minutes to 8 days.

Clinical features (*Table IV*)

Eight patients were unconscious, 2 were semiconscious and one was conscious. Signs of localization by way of aphasia and hemiparesis were noted in 3 cases. No lucid interval was found in any case.

Radiological features

Plain X-rays of the head were taken in 9 patients, of whom 5 had fractures on both sides of the skull. In 3 cases unilateral fractures were found of which one was a depressed fracture. In *Case* 6 no obvious fracture was noticed on radiological examination but prominent venous channels were present, and a linear fracture in the frontal bone was found at autopsy.

Operative findings

The operative and autopsy findings are given in *Table III.* Seven patients were operated upon. In 3 cases it was possible to evacuate the extradural clots on both sides. In *Case* 1 biparietal craniectomy was done, a parietal extradural haematoma was removed and an associated left-sided subdural haematoma was drained, yet the parieto-occipital extension of the extradural haematoma was missed. In *Case* 2 bilateral extradural clots were evacuated; the brain was markedly compressed and the patient died 11 hours after surgery. The parieto-temporal extension was missed. In *Case* 7 a left parietal extradural haematoma was evacuated and on the right side only a small parietal clot was found. The brain did not expand. A parasagittal haematoma was missed. This patient had

---

[*] Department of Neurosurgery, Government General Hospital, Guntur, Andhra Pradesh, India.

Table II: CAUSES OF HEAD INJURY IN REPORTED SERIES

Author	Hospital	Cause of injury (% of cases) Road accident	Fall	Assault
Rowbotham et al. (1954)	Newcastle Hospital, UK	34	22	19
Dayananda Rao et al. (1967)	Osmania General Hospital, Hyderabad, India	34	31	14
Jain and Kankandy (1969)	Irvin Hospital, Delhi, India	43	55	5
Kalyanaraman et al. (1970)	Government General Hospital, Madras, India	47	38	4
Sambasivan and Ramachandran (1973)	Government General Hospital, Trivendrum, India	37	32	18
Present series (1975)	Government General Hospital, Guntur, India	25	7	60

Table III: OPERATION AND AUTOPSY FINDINGS

Case no.	Operation	Autopsy findings Extradural haematoma	Associated injuries
1	Biparietal craniectomy; parietal extradural haematomas removed; left-sided subdural haematoma drained	Parieto-occipito-temporal haematomas Right: 15 × 9 × 2 cm Left: 10 × 9 × 1 cm	1. Laceration of tip of left temporal lobe 2. Contusion of right cortex 3. Pontine haemorrhage 4. Fracture of right parieto-occipital and left parietal bones
2	Biparietal craniectomy; evacuation of parietal clots	Parieto-temporal haematomas Right: 4 × 2 × 1 cm Left: 3 × 2 × 1 cm	Compression of brain
3	Not operated	Bitemporal extradural haematomas Right: 3 × 2 × 1 cm Left: 6 × 6 × 3 cm	1. Left subdural haematoma of 6 × 4 × 3 cm 2. Laceration, 3 × 1 × 1 cm, of the left temporal lobe and base of the frontal lobe 3. Fractures of right parieto-temporal, left parietal and occipital bones. Faciomaxillary fractures on the left side
4	Conventional exploratory burr holes; depressed fracture removed. Laceration of the brain on left parietal lobe noticed	Left fronto-parieto-temporal haematoma of 14 × 7 × 2 cm Right parietal haematoma of 9 × 6 × 2 cm	1. Laceration of left parietal lobe 2. Intracerebral haematoma of left parietal lobe
5	Left parietal craniectomy and evacuation of clot; left subdural haematoma drained. Right temporal burr hole revealed no clot	Left parieto-temporal clot of 9 × 6 × 1 cm Right parietal haematoma of 8 × 6 × 1·5 cm	1. Laceration of the left temporal lobe 2. Laceration of the right frontal lobe 3. Coronal suture diastasis
6	Not operated	Left fronto-temporal clot of 20 × 16 × 8 cm Right temporo-parietal clot 9 × 7 × 6 cm	1. Linear fissured fracture of frontal bone 2. Brain markedly compressed
7	Left temporal craniectomy and evacuation of the clot; small right temporal clot present. Brain did not expand	Parasagittal extradural haematoma of 13 × 12 × 1 cm	1. Laceration, 4 × 3 × 1 cm, of left temporal lobe 2. Brain compressed 3. Sagittal suture diastasis 4. Fracture of both temporal bones
8	Not operated	Left parietal clot of 9 × 8 × 2 cm Right parietal clot of 8 × 6 × 2 cm	1. Extensive scalp haematoma 2. Bifrontal subdural haematoma of 5 × 4 × 2 cm 3. Fracture of occipito-temporal bones of both sides 4. Fracture of base of middle cranial fossa
9	Bilateral exploratory burr holes; depressed fracture removed	Extensive extradural haematomas occupying both sides	1. Extensive scalp haematoma 2. Contusion of corpus callosum and midbrain 3. Brain compressed 4. Fracture of frontal bone extending to both temporoparietal bones
10	Not operated	Extensive extradural haematomas occupying entire extradural space on both sides	1. Subdural haematoma of 150 ml in right frontal region 2. Fracture of frontal bone extending to orbit
11	Bilateral exploratory anterior burr holes	Left pre-frontal extradural haematoma of 6 × 3 × 1 cm Bilateral posterior fossa extradural haematomas	1. Laceration of left frontal lobe 2. Fracture of left frontal bone 3. Fracture of anterior cranial fossa

survived the longest when death occurred 8 days after the injury.

In 4 patients explored by means of conventional burr holes the clots were missed. In 2 of these cases depressed fractures were removed and brain lacerations were found. In *Case* 11 a posterior fossa extradural haematoma was missed as only exploratory burr holes were made because the patient was conscious and aphasic.

Four cases died before any operative intervention, i.e. within a short time of admission.

Autopsy findings

All the cases were submitted to autopsy for forensic reasons. Extensive bilateral extradural haematomas of varying sizes were encountered in association with severe damage to the brain. In most cases the haematomas were parieto-temporal, 2 cases were parasagittal and in 2 cases the collections were diffuse (*Table V*), occupying the entire extradural space on both sides (*Cases* 9, 10). In *Case* 11 left frontal injury with fracture was associated with a left-sided pre-frontal extradural haematoma and a bilateral posterior fossa extradural haemorrhage (*Table III*).

Laceration of the brain was found in 6 cases, subdural haematoma in 4 cases and intracerebral haematoma in 1 case. Pontine haemorrhage in 1 case and contusion of the corpus callosum and the brainstem in another were also found.

Fracture of the skull bones was detected in all the cases during the autopsy examination. Five of these extended to the base of the skull and one fracture was depressed.

Mortality

All the patients in this series died, 4 within a short time of admission and before any neurosurgical intervention. Nine patients had severe associated brain damage. Of the 7 operated cases, 5 had laceration of the brain and in 1 case contusion of the corpus callosum and midbrain. Two patients (*Cases* 2 and 6) who had brain damage other than that due to the bilateral extradural haematomas could have been saved by early operation.

Case 11 was an unusual presentation of bilateral posterior fossa extradural clot where the patient remained conscious and the only clinical feature was aphasia. He was also found to have a pre-frontal extradural clot.

Discussion

Forty-nine cases of extradural haematoma in 1000 patients with head injuries is a high incidence, as is shown in *Table I*. Moreover, 11 cases of bilateral extradural haematomas amount to 22·4 per cent of the total extradural haematomas and 1·1 per cent of the total head injuries.

Assault was responsible for 60 per cent of the head injury cases and 7 out of the 11 bilateral extradural haematomas. In the 53 cases of extradural haematoma reported by Cabraal and Weinman (1964) assault was the main cause in 43·4 per cent.

Table IV: MAIN CLINICAL FEATURES

Clinical feature	No. of cases
Level of consciousness at time of admission:	
Unconscious	8
Semiconscious	2
Conscious	1
Aphasia	3
Hemiparesis	2
Decerebrate response	2
Generalized convulsions	1
Pupillary changes	
Dilated and fixed	5
Paradoxical reaction to light	1
Not significant	5

Table V: SITES OF BILATERAL EXTRADURAL HAEMATOMAS

Site	No. of cases	
	Right	Left
Parietal	3	2
Parieto-temporo-occipital	2	1
Parieto-temporo-frontal	—	2
Parieto-temporal	1	1
Temporal	1	1
Parasagittal	1	1
Diffuse	2	2
Frontal	—	1
Posterior fossa	1	

We may ask ourselves:

1. Why is the incidence of extradural haematoma so high? The only striking factor on reviewing the causes is that assault was responsible for 60 per cent of the cases (*Table II*).

In the series of Dayananda Rao et al. (1967), where also the majority of the cases who died were submitted for post-mortem examination, only 1 case of bilateral extradural haematoma was found out of 4500 cases of head injuries during a period of 6 years.

The age grouping reveals that the incidence is highest in those over 25 years of age. In this connection it is worth noting that the injuries were mostly sustained in 'faction' fights with a view to kill, which may explain the seriousness of the intracranial damage that was found.

2. What lessons may be learnt? In every case of assault the possibility of bilateral extradural haematoma must be borne in mind. In 2 cases extradural haematomas alone were found at post-mortem examination. These cases could have been saved by timely and proper intervention. Although the remaining 9 cases had associated brain damage, evacuation of the clot before the development of irreversible changes could have considerably reduced the mortality.

Routine X-rays failed to reveal the presence of a linear fracture in one case and a depressed fracture in another. At post-mortem all the cases showed evidence of multiple fractures.

The ancillary methods of investigation such as angiography have yet to establish their usefulness in the care of emergency cases in this unit.

Using two conventional burr holes in such serious cases the chances of missing the lesions are great. It is therefore advisable to make at least four exploratory burr holes. The only patient who had a supratentorial frontal extradural haematoma and a posterior fossa clot was clinically conscious and neurologically normal except for aphasia. Conventional burr holes failed to reveal the frontal extradural haematoma. Probably the extent of the posterior fossa clot was not sufficient to cause changes in the vital functions.

Acknowledgements

We are grateful to the Department of Forensic Medicine, Government General Hospital, Guntur, for the details of the post-mortem findings.

We also wish to thank the Superintendent, Government General Hospital, Guntur, for permission to publish this article.

References

CABRAAL S. A. and WEINMAN D. F. (1964) Extradural haematoma. *Neurol. India* **12**, 132–143.

DAYANANDA RAO B., SUBRAHMANIAN M. V., RAGHAVAREDDY M. V. and NAIDU V. B. S. (1967) Mortality in acute head injuries. *Neurol. India* **15**, 1–5.

GALLAGHER J. P. and BROWDER E. J. (1968) Extradural haematoma. Experience with 167 patients. *J. Neurosurg.* **29**, 1–12

HOOPER R. (1959) Observations on extradural haemorrhage. *Br. J. Surg.* **47**, 71–87.

JAIN S. P. and KANKANDY V. D. (1969) A study of 1,500 cases of head injuries in Delhi. *J. Indian Med. Assoc.* **5**, 204–211.

JAMIESON K. G. and YELLAND J. D. N. (1968) Extradural haematoma. Report of 167 cases. *J. Neurosurg.* **29**, 13.

KALYANARAMAN S. and RAMAMURTHI B. (1968) Extradural haemorrhage. *J. Indian Med. Assoc.* **50**, 199–201.

KALYANARAMAN S., RAMAMURTHI B. and RAMANUJAM P. B. (1970) Extradural haemorrhage. *Neurol. India* **18**, Suppl. 1, 12–17.

MCLAURINE R. L. and FORD L. E. (1964) Extradural haematoma. Statistical survey of forty-seven cases. *J. Neurosurg.* **21**, 364–371.

ROWBOTHAM G. F., MACIVER I. N. DICKSON J. and BOUSFIELD M. E. (1954) Analysis of 1,400 cases of acute injury to the head. *Br. Med. J.* **1**, 726–730.

SAMBASIVAN M. and RAMACHANDRAN S. K. (1973) Head injuries. *J. Indian Med. Assoc.* **60**, 120–124.

SONI S. R. (1973) Bilateral asymmetrical extradural haematoma. Case report. *J. Neurosurg.* **38**, 647–649.

Br. J. Surg. Vol. 62 (1975) 401–403

Injury of the facial nerve during surgery of the parotid gland

C. M. WARD*

SUMMARY

The notes of 158 patients who had undergone surgery of the parotid gland for benign and malignant disease were studied to discover the circumstances in which the facial nerve might be injured.

Limited surgery carried as great a risk of injury to the facial nerve as during extended surgery. Extended surgery provided greater risk of injury to the facial nerve on secondary exploration (71 per cent) than on primary exploration (6·5 per cent).

It is concluded that every primary exploratory procedure of the parotid gland should be a formal conservative parotidectomy unless the tumour is obviously malignant.

THE principle of surgery of the parotid gland is adequate removal of the tumour with functional and anatomical preservation of all branches of the facial nerve whenever possible. This principle has been emphasized and re-emphasized since surgery of the parotid gland became a reasonable proposition, yet little is written of the incidence of injury to the facial nerve. This paper reviews the results of operations on the parotid gland noting the circumstances of injury to the facial nerve.

Patients and methods

Between 1963 and 1972 158 patients with lesions of the parotid gland were treated surgically by the consultant and junior staff in the Departments of Ear, Nose and Throat Surgery, General Surgery and Plastic Surgery, Frenchay Hospital, Bristol.

The usual classification of peripheral nerve injury, namely neuropraxia, axonotmesis and neurotmesis, is difficult to apply in this study as several of the patients had been referred from counties remote to Frenchay Hospital. These patients were seen in their own district hospitals after a more limited local follow-up than applied to patients referred from the more immediate vicinity of Frenchay Hospital. Therefore, in the context of this retrospective study, injury to the facial nerve is defined as damage to one or more branches leading to unacceptable functional or cosmetic disability that may or may not recover after 6 months following surgery. This definition takes no account of neuropraxia but embraces neurotmesis and axonotmesis without distinguishing between them. The distress of the patient, however, is no less in that time whether the axon or the neuron of the facial nerve has been ruptured.

The operations performed were very variable but basically fall into five groups. These are: enucleation, removal of the tumour with a cuff of normal tissue, removal of the lower pole of the parotid gland, superficial parotidectomy, which may be extended if the tumour is found in the deep lobe, and total parotidectomy with or without deliberate sacrifice of the facial nerve. The first three groups involve procedures in which the trunk of the facial nerve is not identified. The techniques can therefore be classified more simply by: (1) limited surgery, (2) conservative formal parotidectomy and (3) total parotidectomy.

No attempt has been made to differentiate between the types of malignant tumour nor has an attempt been made to study in detail the recurrence of these tumours or pleomorphic adenomas in relation to surgical technique.

Table I: COMPARISON OF THE PRESENT SERIES WITH THAT OF ENEROTH (1966)

	Frenchay Hospital 1963–72 ($n = 158$)		Karolinska Sjukhuset 1950–62 ($n = 802$)
Type of tumour	No.	%	
Benign	126	79·7	83·4
Pleomorphic adenoma	89	56·2	69·0
Adenolymphoma	14	8·8	5·0
Oxyphilic adenoma	1	0·6	1·0
Benign lympho-epithelioma	2	1·3	0·8
Mesenchymal tumours	2	1·3	1·5
Pseudotumours	18	11·4	6·1
Malignant	32	20·3	16·6

Table II: INJURY TO THE FACIAL NERVE DURING SURGERY OF PLEOMORPHIC ADENOMAS

Treatment	No. of cases	Injury to facial nerve
Limited surgery	22	0
Limited surgery after previous surgery	2	1
Conservative formal parotidectomy	52	0
Conservative formal parotidectomy after previous surgery	13	9
Total parotidectomy	2	0
Total	91	10

Results

Thirty-two patients (20·3 per cent) had malignant disease of the parotid gland while 126 (79·7 per cent) had benign lesions. The main difference in these figures from those of the Karolinska Sjukhuset (Eneroth, 1966) is the lower proportion of pleomorphic adenomas and the higher proportion of pseudotumours (*Table I*).

---

* Department of Plastic Surgery, Frenchay Hospital, Bristol. Present address: Wessex Centre for Plastic and Maxillofacial Surgery, Odstock Hospital, Salisbury.

Injury to the facial nerve during surgery of the pleomorphic adenomas is shown in *Table II* and during surgery of other benign lesions in *Table III*. In *Table IV* it is very apparent that previous surgery of the parotid gland for benign disease leads to a greater risk of injury to the facial nerve on subsequent exploration regardless of the surgical procedure adopted.

The results of surgery of malignant tumours of the parotid gland in *Table V* show that of 13 patients without previous treatment, 2 had facial nerve injuries, whereas of 4 patients previously treated, 3 had nerve injuries at subsequent operations.

Considering all the patients in whom attempts were made to preserve the facial nerve, 8 out of 124 (6·5 per cent) had facial nerve injuries from primary surgery while 15 out of 21 (71 per cent) had facial nerve injuries from secondary surgery.

Discussion

It is difficult to compare results of surgery on the parotid gland. The reports differ greatly from an individual who takes a particular interest in the treatment of disease of the parotid gland and who would therefore have better results than those of a group of surgeons of variable experience for whom surgery of the parotid gland is not necessarily a special interest. Furthermore, the definition of injury to the facial nerve differs according to the duration of follow-up of the patient and to the grade of paralysis, which is a subjective observation. Thus, of a personal series of 105 patients with pleomorphic adenomas treated by total conservative parotidectomy (Kidd, 1969), there were no permanent paralyses except where a branch of the nerve was deliberately sacrificed, while for a group of surgeons (Gore et al., 1964) 7 out of 35 patients developed facial paresis lasting more than 3 months from surgical techniques varying from limited to more extensive procedures.

In a detailed analysis of functional paralysis of the facial nerve following parotidectomy (Patey and Moffat, 1961) the paralyses were graded into three groups of which grade III failed to improve until 2–6 months after operation. Of 31 patients primarily treated by total conservative parotidectomy, 9 (29 per cent) developed grade III paresis, while of 64 patients treated by superficial parotidectomy, 4 (6 per cent) developed the same degree of facial weakness.

Limited surgery such as enucleation may occasionally be considered as a safer procedure or even the treatment of choice for a benign parotid tumour (Guras et al., 1973), yet in this series (*Table IV*) 3 out of 40 benign lesions treated primarily by limited procedures developed facial paresis compared with 2 out of 67 benign lesions treated primarily by conservative formal parotidectomy. It therefore appears that the facial nerve and its branches are as much at risk during limited surgery as during extended surgery. No matter how limited might be the surgical procedure adopted during exploration of a parotid tumour, every branch must be carefully identified and preserved.

Table III: INJURY TO THE FACIAL NERVE DURING SURGERY OF BENIGN LESIONS

Type of tumour	Treatment	No. of cases	Injury to facial nerve
Adenolymphoma	Limited surgery	10	2
	Limited surgery after radiotherapy	1	1
	Conservative formal parotidectomy	3	0
Oxyphilic adenoma	Limited surgery	1	0
Benign lympho-epithelioma	Limited surgery	1	1
	Conservative formal parotidectomy	1	0
Mesenchymal tumours			
Lipoma	Conservative formal paratidectomy	1	1
Lymphohaem-angioma	Conservative formal paratidectomy after previous surgery	1	1
Sialectases	Limited surgery	2	0
	Conservative formal parotidectomy	5	0
	Total parotidectomy	2	1
Cysts	Limited surgery	3	0
	Conservative formal parotidectomy	4	1
Calculi	Limited surgery	1	0
	Conservative formal parotidectomy	1	0
	Total	37	8

Table IV: INJURY TO THE FACIAL NERVE DURING SURGERY OF ALL BENIGN LESIONS

Treatment	No. of cases	Injury to facial nerve
Limited surgery	40	3
Limited surgery after previous surgery	3	2
Conservative formal parotidectomy	67	2
Conservative formal parotidectomy after previous surgery	14	10
Total parotidectomy	4	1

Table V: INJURY TO THE FACIAL NERVE DURING SURGERY OF MALIGNANT TUMOURS

Treatment	No. of cases	Injury to facial nerve
Limited surgery	3	0
Conservative formal parotidectomy	6	0
Conservative formal parotidectomy after previous surgery	2	1
Total parotidectomy with attempts to preserve the facial nerve in 4 cases	15*	2
Total parotidectomy after previous surgery with attempts to preserve the facial nerve in 2 cases	3†	2

* Eight patients had preoperative paresis.
† One patient had preoperative paresis.
Radiotherapy was given to 2 patients with anaplastic carcinoma and to 1 patient with adenocarcinoma who refused an operation.

It is known that there is a significant recurrence of pleomorphic adenomas after limited surgery (Leading Article, 1972; Hugo et al., 1973). In the present series (*Table II*) 9 out of 13 patients with pleomorphic adenoma treated secondarily by conservative formal parotidectomy had injuries of the facial nerve. Of a personal series of 100 patients with pleomorphic adenoma treated by superficial parotidectomy (Eddey, 1970), 15 had had previous limited surgery of which

20 per cent developed permanent facial paralysis. Therefore it becomes apparent that a benign tumour of the parotid gland should be treated by extended surgery not only to reduce any chance of recurrence but also to prevent risk of injury to the facial nerve that is more likely during reoperation for a recurrence after limited surgery.

Several factors are responsible for the increased susceptibility of the facial nerve to injury during multiple operations on the parotid gland. Ischaemic anoxia of the nerve as a result of surgical interference with the vasa nervorum is quoted (Patey and Moffat, 1961). In fact, these authors, using the experimental model of the rabbit, found that by direct blunt trauma of the facial nerve it was difficult to produce paralysis. The mechanism of ischaemia applies to primary surgery but more obviously to secondary surgery when the facial nerve is stripped of the few blood vessels that may remain in the adherent scar tissue resulting from previous interference. In this same situation it becomes more difficult to recognize and to trace the branches of the facial nerve, thereby resulting in inadvertent direct trauma. After recurrence of either a malignant tumour or a pleomorphic adenoma the clearance required to reduce the likelihood of a further recurrence often implies deliberate sacrifice of a branch of the facial nerve. Furthermore, in the presence of scar tissue from previous surgery it may be easy to confuse recurrence with fibrosis.

Accurate diagnosis of a parotid tumour on clinical assessment alone is notoriously difficult unless there is obvious evidence of its malignant nature such as invasion of neighbouring structures, facial palsy or metastases, yet even a benign tumour can lead to a facial palsy (Wilkie and White, 1969). Those who have the special experience required of fine needle biopsy can plan treatment according to the preoperative diagnosis (Eneroth, 1964; Eneroth and Zajiceck, 1965). Indeed, aspiration biopsy by fine needle is regarded as an essential preliminary to surgical treatment (Webb, 1974). Others (Janes, 1957; Patey and Thackray, 1958) consider that previous knowledge of the nature of the tumour would not influence their surgical treatment and that cell spillage and implantation is too great a risk. From the relatively low incidence of injury of the facial nerve (6·5 per cent) during primary extended surgery of both benign and malignant tumours (*Tables IV, V*) it would seem justifiable to treat all lesions of the parotid gland by conservative formal parotidectomy unless clinically they are obviously malignant. If during this operation it is apparent on the evidence of frozen section or from the appearance of the tumour that it is malignant the surgical procedure should be adjusted accordingly. However, it is emphasized in the light of these findings that every exploratory procedure of the parotid gland should be a conservative formal parotidectomy, not only to cure 85 per cent of all patients with parotid tumours (Patey, 1966) but also to avoid the much greater chance of injuring the facial nerve during secondary surgery.

Acknowledgements

I would like to thank Mr D. C. Bodenham, Mr L. R. Celestin, Mr C. M. Davidson, Mr N. Edwards, Mr H. Fairman, Mr G. M. Fitzgibbon, Mr R. W. Hiles, Mr R. E. May, Mr R. W. Pigott and Mr R. T. Routledge for permission to include their patients in this study.

References

EDDEY H. H. (1970) Recurrent parotid tumours. *Aust. NZ J. Surg.* **39**, 356–361.

ENEROTH C. M. (1964) Histological and clinical aspects of parotid tumours. *Acta Otolaryngol.* (*Suppl.* 191) (*Stockh.*)

ENEROTH C. M. (1966) Classification of parotid tumours. *Proc. R. Soc. Med.* **59**, 429–435.

ENEROTH C. M. and ZAJICECK J. (1965) Aspiration biopsy of salivary gland tumours. *Acta Cytol.* (*Baltimore*) **9**, 355–361.

GARAS J., POLITIS A., BESBEARS S., GEORGACAS G. and PAPAMATHEAKIS J. (1973) Neoplasm of the parotid gland: review of 185 operated cases. *Int. Surg.* **59**, 178–181.

GORE D., ANNAMUNTHODO H. and HARLAND A. (1964) Tumours of salivary gland origin. *Surg. Gynecol. Obstet.* **119**, 1290–1295.

HUGO N. E., MCKINNEY P. A. and GRIFFITH B. H. (1973) Management of tumours of the parotid gland. *Surg. Clin. North Am.* **53**, 105–111.

JANES R. M. (1957) Tumours of the parotid gland. *Ann. R. Coll. Surg.* **21**, 1–12.

KIDD H. A. (1969) Diseases of the parotid and the Frey syndrome. *Br. J. Hosp. Med.* **2**, 1513–1522.

LEADING ARTICLE (1972) Tumours of the salivary glands. *Br. Med. J.* **4**, 252.

PATEY D. H. (1966) The treatment of tumours of the parotid gland. *Proc. R. Soc. Med.* **59**, 435–436.

PATEY D. H. and MOFFAT W. (1961) A clinical and experimental study of functional paralysis of the facial nerve following conservative parotidectomy. *Br. J. Surg.* **48**, 435–440.

PATEY D. H. and THACKRAY A. C. (1958) The treatment of parotid tumours in the light of a pathological study of parotidectomy material. *Br. J. Surg.* **45**, 77–87.

WEBB A. J. (1974) Personal communication.

WILKIE T. F. and WHITE R. A. (1969) Benign parotid tumour with facial nerve paralysis. *Plast. Reconstr. Surg.* **43**, 528–530.

Br. J. Surg. Vol. 62 (1975) 404–406

Recognition of infection associated with intravenous catheters

R. FREEMAN AND B. KING*

SUMMARY

Four cases are described in which the patients suffered from bacteriaemia due to infected intravenous infusions. Although all the patients were pyrexial, the white cell count was normal in all 4 cases at diagnosis and the infusion site appeared innocent.

Following removal of the intravenous catheter and the institution of antibiotic therapy in each case, neutrophilia and localizing signs developed. It is stressed that a normal white cell count and an innocent appearance at the infusion site do not exclude this complication of intravenous therapy. Possible reasons for this presentation of sepsis are discussed.

INFECTIVE complications of indwelling intravenous catheters have recently been recognized as a potential hazard in any patient requiring prolonged intravenous therapy (Freeman and King, 1972; Cox, 1973). This is particularly so in patients receiving parenteral nutrition—so called 'intravenous feeding' (Ashcraft and Leape, 1970; Curry and Quie, 1971). We describe the following cases to emphasize one way in which infective complications may present.

Case reports

Case 1: A 33-year-old woman who underwent laparotomy for intestinal obstruction developed paralytic ileus postoperatively. She required prolonged intravenous therapy, and on the third day of this régime her general condition deteriorated. The main features of her illness were fever, tachycardia and a feeling of general malaise, associated with some nausea. The intravenous fluids being given were simple electrolytes (normal saline, dextrose-saline and 5 per cent dextrose solutions). She did not receive any hypertonic amino-acid or lipid preparations. The illness continued for 48 hours, during which time the white cell count remained normal and the infusion site appeared unremarkable, apart from mild hyperaemia. Blood cultures were taken and the patient was given parenteral gentamicin (80 mg 8-hourly). Only marginal improvement occurred over the next 24 hours, but a rapid resolution followed the removal of the intravenous catheter. Within 3–4 hours the temperature had fallen to normal levels and the tachycardia abated overnight. The patient admitted to feeling much better.

Over the next 3 days the white cell count rose, and a neutrophil leucocytosis developed. Five days after the removal of the intravenous catheter a large abscess had appeared at the infusion site, and this was evacuated. Culture of the contents revealed *Staphylococcus aureus*, and this organism was also subsequently reported to be present in the blood cultures. Antibiotics were continued for a further period to minimize the risk of endocarditis.

Case 2: A man aged 45 years suffered multiple injuries in a road traffic accident and required parenteral nutrition. In the second week of this therapy he developed a hectic fever with no obvious source of infection. A chest X-ray, urine examination and the white cell count were all unhelpful. In particular, the white cell count was found to be normal, with a normal differential count. One of the infusion sites showed slight erythema. Blood cultures were taken and the catheter was removed, the severed tip being sent for culture. Both the blood cultures and the catheter tip culture yielded *Staph. aureus*, and the patient was immediately given cloxacillin at a dose of 500 mg intramuscularly 6-hourly. The temperature rapidly settled and this was associated with a rise in the white cell count and the development of a neutrophil leucocytosis. The site of the infusion developed into a large abscess requiring drainage whilst he was being treated for his septicaemia. The evacuated pus was sterile on culture.

Unfortunately, the patient eventually died as a result of renal failure which had complicated his other injuries.

Case 3: A 55-year-old man was receiving parenteral nutrition with amino-acid solutions and lipid suspensions whilst recovering from major abdominal surgery for ulcerative colitis, complicated by paralytic ileus. On the fifth day of this régime he became febrile and unwell. No source of sepsis was found and the white cell count remained normal. The infusion site was slightly erythematous and there was some thrombosis of the vein. Blood cultures yielded *Staph. aureus*, and treatment with lincomycin 500 mg intramuscularly 6-hourly and cloxacillin 500 mg intramuscularly 6-hourly was given. There was little improvement over the following 3 days, during which time he was noted to have several rigors, but a rapid fall in temperature and a gradual improvement in his general condition occurred after removal of the intravenous catheter. Culture of the catheter tip was negative, but the infusion site developed into an abscess shortly afterwards and culture of the pus obtained from this lesion produced a scanty growth of *Staph. aureus*. Following the removal of the catheter the white cell count revealed a neutrophil leucocytosis.

Case 4: A man aged 30 years was admitted following a road traffic accident, having sustained multiple injuries. Prolonged intravenous feeding was given, but after 6 days the patient began to show a low grade pyrexia which persisted. Careful inspection of the infusion sites revealed no abnormality and the white cell count was normal. The white cell count had been slightly elevated at admission but had returned to normal within 3 days. The catheter tip was removed for culture and this produced a heavy growth of *Staph. albus* (coagulase negative), but owing to doubts about its significance no specific therapy was given until blood cultures revealed the same organism. Therapy with cloxacillin 500 mg intramuscularly 6-hourly was commenced although the patient was by that time afebrile. Over the 2 days following removal of the catheter the white cell count developed a neutrophil leucocytosis, and the infusion site developed cellulitis, but this resolved without suppuration.

Discussion

These 4 cases illustrate a presentation of sepsis following intravenous infusions which is characteristic once recognized, but which is easily overlooked. A summary of the details of the cases is given in *Tables I* and *II*. The important features are:

1. The infusion site may look quite innocent, exhibiting only a slight erythema over the vein, and certainly not showing any sign that it is the source of a septicaemia.

2. The white cell count is characteristically normal, in both total count and differential count. This may

---

* Department of Microbiology, University of Leeds.

Table I: APPEARANCE OF THE INFUSION SITE AND THE WHITE BLOOD CELL COUNT

Case	White blood count (cells/mm^3)		Appearance of infusion site	
	At diagnosis	Third day of therapy	At diagnosis	Third day of therapy
1	$5{\cdot}6\times10^3$, diff. normal	$16{\cdot}5\times10^3$, neutrophilia	Mild hyperaemia	Abscess forming
2	$6{\cdot}7\times10^3$, diff. normal	$18{\cdot}4\times10^3$, neutrophilia	Slight erythema	Abscess forming
3	$3{\cdot}4\times10^3$, diff. normal	$17{\cdot}0\times10^3$, neutrophilia	Erythema and thrombosis	Abscess forming
4	$7{\cdot}5\times10^3$, diff. normal	$18{\cdot}3\times10^3$, neutrophilia	No apparent abnormality	Cellulitis

Table II: ORGANISMS ISOLATED AND THEIR ANTIBIOTIC SUSCEPTIBILITIES

Case	Organism isolated		Therapy given and sensitivity pattern of organism
	Blood	Local site	
1	*Staph. aureus*	*Staph. aureus* (pus)	Sens.: Clox., linco., fuc., genta., cep. Res.: Pen., amp., tet. Given: Genta. 80 mg t.d.s.
2	*Staph. aureus*	*Staph. aureus* (catheter tip)	Sens.: Clox., linco., fuc., cep., tet. Res.: Pen., amp. Given: Clox. 500 mg q.d.s.
3	*Staph. aureus*	*Staph. aureus* (pus)	Sens.: Clox., linco., fuc., cep., tet. Res.: Pen., amp. Given: Clox. 500 mg+linco. 600 mg both q.d.s.
4	*Staph. albus*	*Staph. albus*	Sens.: Clox., fuc., cep. Res.: Pen., amp., linco. Given: Clox. 500 mg q.d.s.

Sens., Sensitive to. Res., Resistant to. Pen., Pencillin. Amp., Ampicillin. Linco., Lincomycin. Fuc., Fucidin. Clox., Cloxacillin. Cep., Cephaloridine. Tet., Tetracycline. Genta., Gentamicin.

not only lead the investigation away from the infusion site, but may even give the impression that the patient's illness is not even infective.

3. Following the recognition of the complication, effective therapy consists of both chemotherapy and removal of the catheter. *Cases* 1 and 3 suggest that chemotherapy alone may not succeed until the foreign material is removed.

4. The catheter having been removed and chemotherapy having been started, the white cell count rises and a neutrophil leucocytosis develops. Suppuration or cellulitis follows at the infusion site.

All these cases have one other feature in common: the infusion was administered in each case via an indwelling intravenous catheter. Previous work has shown that such catheters frequently yield an organism when the tip is cultured, and that this is more likely to occur when the catheter has been *in situ* for more than 2 days (Freeman and King, 1972). The route by which the organisms gain access is still uncertain, but the fact that indwelling intravenous catheters become infected is now well recognized. What is notable about the patients described here is their apparent lack of host response, both locally at the infusion site and generally as expressed by the white cell count. Three factors may be concerned. First, the nature of the infective lesion is similar to that found in infective endocarditis. Thus, there is an infected focus in the major bloodstream which the body is unable to supply with inflammatory cells since there is no blood supply to the lesion. It is noteworthy that a normal white cell count is often found in endocarditis (Weinstein and Rubin, 1973). Secondly, indwelling intravenous catheters are yet another example of foreign material implanted in the body. Indeed, they are probably the commonest instance of this. There is thus a parallel with infections of other prosthetic implants. It is characteristic of the infections complicating Spitz–Holter valves in hydrocephalic children that there is a lack of inflammatory response in the cerebrospinal fluid despite the easy isolation of bacteria (Cohen and Callaghan, 1961). These infections often require the removal of the foreign material to control them.

Thirdly, recent work has suggested that in patients receiving prolonged parenteral nutrition, depletion of body phosphate may occur, leading to a diminished chemotaxis and bactericidal power in the neutrophils (Craddock et al., 1974). Thus, the host resistance may be diminished in these patients. However, one of our cases received only crystalloid, and in all the cases recovery occurred without phosphate repletion. Since phosphate studies and neutrophil function tests were not carried out on our patients we are unable to prove that these abnormalities were not present, but this last factor is unlikely in these cases in view of the response to treatment and the very rapid local and general inflammatory reaction which ensued.

Finally, it should be stressed that in a patient receiving prolonged intravenous therapy, infection arising from the infusion site should always be considered as a likely cause of an unexplained pyrexia. If the white cell count is normal, infection of this site is probably more likely than infection elsewhere. The infection rate can be reduced by early removal of the catheter or by rotation of sites (Freeman et al., 1973), and the infected catheter may be detected by serial nitroblue tetrazolium (NBT) tests (Freeman and King, 1972; Freeman et al., 1973).

References

ASHCRAFT K. W. and LEAPE L. L. (1970) Candida sepsis complicating parenteral feeding. *JAMA* **212**, 454–456.

COHEN S. J. and CALLAGHAN R. P. (1961) A syndrome due to the bacterial colonisation of Spitz–Holter valves. *Br. Med. J.* **2**, 677–679.

COX G. E. (1973) Bacterial contamination of drip sets. *NZ Med. J.* **77**, 390–394.

CRADDOCK P. R., YAWATA Y., VANSANTEN L., GILBERSTADT S., SILVIS S. and JACOB H. S. (1974) Acquired phagocyte dysfunction—a complication of the hypophosphataemia of parenteral hyperalimentation. *New Engl. J. Med.* **290**, 1403–1407.

CURRY C. R. and QUIE P. G. (1971) Fungal septicaemia in patients receiving parenteral hyperalimentation. *New Engl. J. Med.* **285**, 1221–1225.

FREEMAN R. and KING B. (1972) Infective complications of indwelling intravenous catheters and the monitoring of infections by the NBT test. *Lancet* **1**, 992–993.

FREEMAN R., KING, B. and HAMBLING M. H. (1973) Infective complications of open-heart surgery and the monitoring of infections by the NBT test. *Thorax* **28**, 617–621.

WEINSTEIN L. and RUBIN R. H. (1973) Infective endocarditis—1973. *Progr. Cardiovasc. Dis.* **16**, 239–274.

Erratum

British Journal of Surgery, Vol. 62 : No. 3 : March 1975, p. 195. The first sentence of the legend to *Fig.* 2 should read: Photomicrograph of regenerating liver at 72 hours after partial hepatectomy showing double cell plates.

Br. J. Surg. Vol. 62 (1975) 407–408

Pilonidal sinus treated by phenol injection

B. A. SHOREY*

SUMMARY
The method of using phenol injections for the treatment of pilonidal sinus is described in detail. This is a simple, safe and painless method which may be used as a day case procedure. The results are discussed and compare very favourably with the more radical forms of treatment.

THE first reported case of a pilonidal sinus that was successfully treated was described by Anderson (1847). The sinus was incised and the enclosed hair removed. Since that time many papers have appeared on the aetiology and treatment of this condition.

It was originally thought that the aetiology was congenital due either to remnants of neural canal becoming separated or to ectodermal inclusions (Mallory, 1892; Kooistra, 1942). However, since the papers of King (1946), showing that the hairs present in these sinuses have their roots nearest the opening, and of Patey and Scarff (1946), describing pilonidal sinus in the interdigital clefts of barbers, the acquired theory of aetiology has become generally accepted. Brearley (1955) and Raffman (1959) also contributed papers supporting the acquired theory and suggesting ways in which the hairs enter the skin.

Pilonidal sinuses have now been reported in many areas of the body—perineum (Smith, 1948), umbilicus (Steck and Helwig, 1965), interdigital cleft (Currie et al., 1953), scalp (Stevens and Anderson, 1961), amputation stump (Shoesmith, 1953), axilla (Aird, 1952). It would thus seem impractical to think of this condition as congenital.

Method

The method used for phenol injection is similar to that first described by Maurice and Greenwood (1964). Following general anaesthesia with endotracheal intubation, the patient is placed prone on the operating table. The table is then raised in the centre or the patient lifted on to pillows to obtain the 'jack-knife' position. The patient, having previously been shaved from the waist to mid-thigh posteriorly, has the buttocks held apart by the use of 7·5-cm strapping, thus exposing the natal area and anal verge. At this stage further shaving may be necessary, especially deep in the natal cleft. The area is now prepared and towelled up in the normal manner. A swab or large piece of cotton wool is used to protect the anus, while the rest of the area is liberally coated with paraffin jelly (Vaseline) to protect it from the phenol.

After careful probing any loose hairs are removed with forceps from the sinus and any of its side tracts. With a blunt needle which fits snugly into the sinus orifice and a 10-ml syringe, the sinus is injected with a solution of 80 per cent phenol. No excess pressure is used for fear of the phenol being forced into the surrounding tissue lining the sinus and causing a local inflammatory reaction.

It has been suggested (Stephens and Sloane, 1969) that the operator should wear glasses as protection against any splash of phenol. This problem did not arise in the present series. On commencing the injection, phenol can be seen issuing from the side canals. The phenol is left *in situ* for 2 minutes and then expressed by pressure. The excess is mopped away with the debris. This manœuvre is repeated two or three times; the orifice of the sinus is seen to blanch at this stage.

A dressing of paraffin jelly is applied, the excess Vaseline being removed. The patient is allowed home when he has recovered from the anaesthetic.

Results

In the Bristol Royal Infirmary during the period 1968–72, 253 patients with pilonidal sinus came to surgery. Various forms of treatment were undertaken as shown in *Table I*.

Table I: METHODS OF TREATMENT OF PILONIDAL SINUSES

	Laying open	Primary suture	Brush technique	Phenol injection
No. of patients	179	42	9	23
No. of failures or recurrences	14	7	2	2

Although those treated by phenol injection comprise only a small percentage of the total, it can be seen that the results compare favourably with those of other methods.

Of the 23 patients so far treated, 20 were male and 3 female; their ages ranged from 18 to 59 years. The presenting symptoms were recurrent abscess formation or a persistent discharge; most of the patients had been having symptoms for over a year.

Successful treatment was judged by epithelization occurring without any discharge or pain; 21 cases were deemed a success while 2 were failures. Of the 2 failures, one was at first successful but recurrence occurred after 9 months with a further abscess. The other case proved very difficult and was resistant to any form of treatment. Phenol injections failed twice and he subsequently had 6 other operations. It was emphasized to all the patients that postoperatively the natal cleft must be kept free of hair by shaving. Personal hygiene of the area was also encouraged.

---

* Department of Surgery, Bristol Royal Infirmary.

Discussion

A large number of operations have been described for the treatment of pilonidal sinuses and all have their supporters. Some of the procedures that have been described for this relatively minor condition are major undertakings, and it is not surprising that Walters and MacDonald (1958) suggested a return to simple treatment. Phenol injection is a simple procedure and offers many advantages to the patient. The length of hospitalization is minimal; all the patients in this series were discharged on the day following operation. It would therefore be a logical step to treat all pilonidal sinuses as day cases, for there is little danger after recovery from the anaesthetic. In fact, 4 patients treated by Stephens and Sloane (1969) had phenol injections as outpatients without a general anaesthetic.

Following phenol injection patients have very little discomfort and are thus able to return to a normal routine almost immediately. Other simple forms of treatment such as marsupialization are widely practised but healing is prolonged; an average of 86 days was quoted by Berkowitz (1949). This leads to discomfort, excess hospitalization, frequent dressings, prolonged medical supervision and more time off work.

Primary excision and closure has many advocates (Holman, 1946; Mandel and Thomas, 1972; Casten et al., 1973), and in good hands very satisfying results are obtained, but failures occur (Rogers and Hall, 1935), hospitalization is longer and postoperative discomfort more severe than with phenol injections. The most drastic operation of rotational flaps has not been popular owing to the length of stay in hospital and postoperative pain. However, good results have been obtained (Davis and Starr, 1945).

The simpler methods of treatment, such as diathermy coagulation (Jacobsen, 1959; Flannery and Kidd, 1967) and incision and brush technique (Lord and Millar, 1965), have the disadvantage that in each technique an incision is made over the sinus. This means that postoperatively the wound has to be dressed and frequent medical supervision is required. However, phenol injection (Maurice and Greenwood, 1964; Stephens and Sloane, 1968; Stewart and Bell, 1969) has several advantages. The operation is simple and the only postoperative dressing required is small, its purpose being to prevent any excess phenol being expressed on to the skin.

Acknowledgement

I would like to thank Mr H. K. Bourns for allowing me to study the patients under his care and for his encouragement in writing this paper.

References

AIRD I. (1952) Pilonidal sinus of the axilla. *Br. Med. J.* **1**, 902–903.

ANDERSON A. W. (1847) Hair extracted from an ulcer. *Bost. Med. Surg. J.* **36**, 74.

BERKOWITZ J. (1949) Sacrococcygeal pilonidal cyst. *Am. J. Surg.* **77**, 477–490.

BREARLEY R. (1955) Pilonidal sinus: a new theory of origin. *Br. J. Surg.* **43**, 62–68.

CASTEN D. F., TAN B. Y. and AYUYAO A. (1973) A technique of radical excision of pilonidal disease with primary closure. *Surgery* **73**, 109–114.

CURRIE A. R., GIBSON T. and GOODALL A. L. (1953) Interdigital sinuses of barber's hand. *Br. J. Surg.* **41**, 278–286.

DAVIS L. S. and STARR K. W. (1945) Infected pilonidal sinus. *Surg. Gynecol. Obstet.* **81**, 309–319.

FLANNERY B. P. and KIDD H. A. (1967) A review of pilonidal sinus lesions and a method of treatment. *Postgrad. Med. J.* **43**, 353–358.

HOLMAN E. (1946) Pilonidal sinus—treatment by primary closure. *Surg. Gynecol. Obstet.* **83**, 94–100.

JACOBSEN P. (1959) Pilonidal disease. Management without excision. *Am. Acad. Gen. Practice* **19**, 84–90.

KING E. S. J. (1946) The nature of the pilonidal sinus. *Aus. NZ J. Surg.* **16**, 182–192.

KOOISTRA H. P. (1942) Pilonidal sinuses, review of literature and report of 350 cases. *Am. J. Surg.* **55**, 3–17.

LORD P. H. and MILLAR D. M. (1965) Pilonidal sinus: a simple treatment. *Br. J. Surg.* **52**, 298–300.

MALLORY F. B. (1892) Sacro-coccygeal dimples, sinuses and cysts. *Am. J. Med. Sci.* **103**, 263–277.

MANDEL S. R. and THOMAS C. G. (1972) Management of pilonidal sinus by excision and primary closure. *Surg. Gynecol. Obstet.* **134**, 448–450.

MAURICE B. A. and GREENWOOD R. K. (1964) A conservative treatment of pilonidal sinus. *Br. J. Surg.* **51**, 510–512.

PATEY D. H. and SCARFF R. W. (1946) Pathology of postanal pilonidal sinus: its bearing on treatment. *Lancet* **2**, 484–486.

RAFFMAN R. A. (1959) A re-evaluation of the pathogenesis of pilonidal sinus. *Ann. Surg.* **150**, 895–903.

ROGERS H. and HALL H. G. (1935) Pilonidal sinus—surgical treatment and pathological structure. *Arch. Surg.* **31**, 742–766.

SHOESMITH J. B. (1953) Pilonidal sinus in an above-knee amputation stump. *Lancet* **2**, 378–379.

SMITH T. E. (1948) Anterior or perineal pilonidal cysts. *JAMA* **136**, 973–975.

STECK W. D. and HELWIG E. B. (1965) Umbilical granulomas, pilonidal disease, and the urachus. *Surg. Gynecol. Obstet.* **120**, 1043–1057.

STEPHENS F. O. and ANDERSON W. A. (1961) Pilonidal sinus of the occipital region. *Med. J. Aust.* **2**, 518.

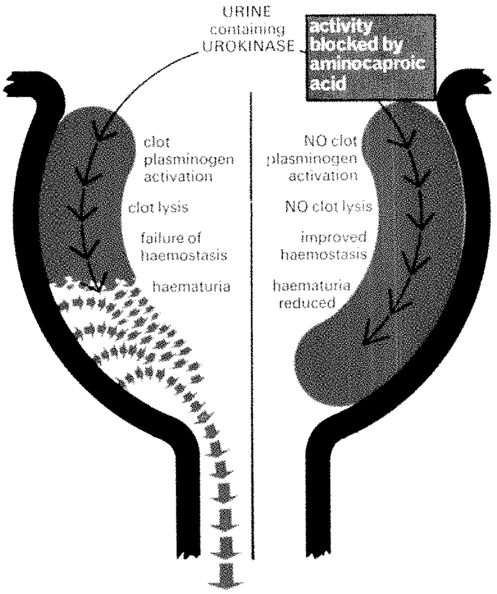
STEPHENS F. O. and SLOANE D. R. (1968) Management of pilonidal sinus—modern approach. *Med. J. Aust.* **1**, 395–396.

STEPHENS F. O. and SLOANE D. R. (1969) Conservative management of pilonidal sinus. *Surg. Gynecol. Obstet.* **129**, 786–788.

STEWART T. J. and BELL M. (1969) The treatment of pilonidal sinus by phenol injection. *Ulster Med. J.* **38**, 167–171.

WALTERS N. and MACDONALD I. B. (1958) Marsupialisation of pilonidal sinus and abscess, a report of 50 cases. *Can. Med. Assoc. J.* **79**, 236–240.

The mechanism of post-prostatectomy bleeding and EPSIKAPRON® control



Epsikapron (aminocaproic acid) is rapidly excreted in the urine in high concentration ; there it inhibits urokinase, the fibrinolytic enzyme in urine. With the haemorrhage-sustaining property of urine blocked, the haemostatic coagulum becomes adequate, and blood loss is diminished substantially.

Epsikapron makes your prostatectomy patient's post-operative course smoother by diminishing :

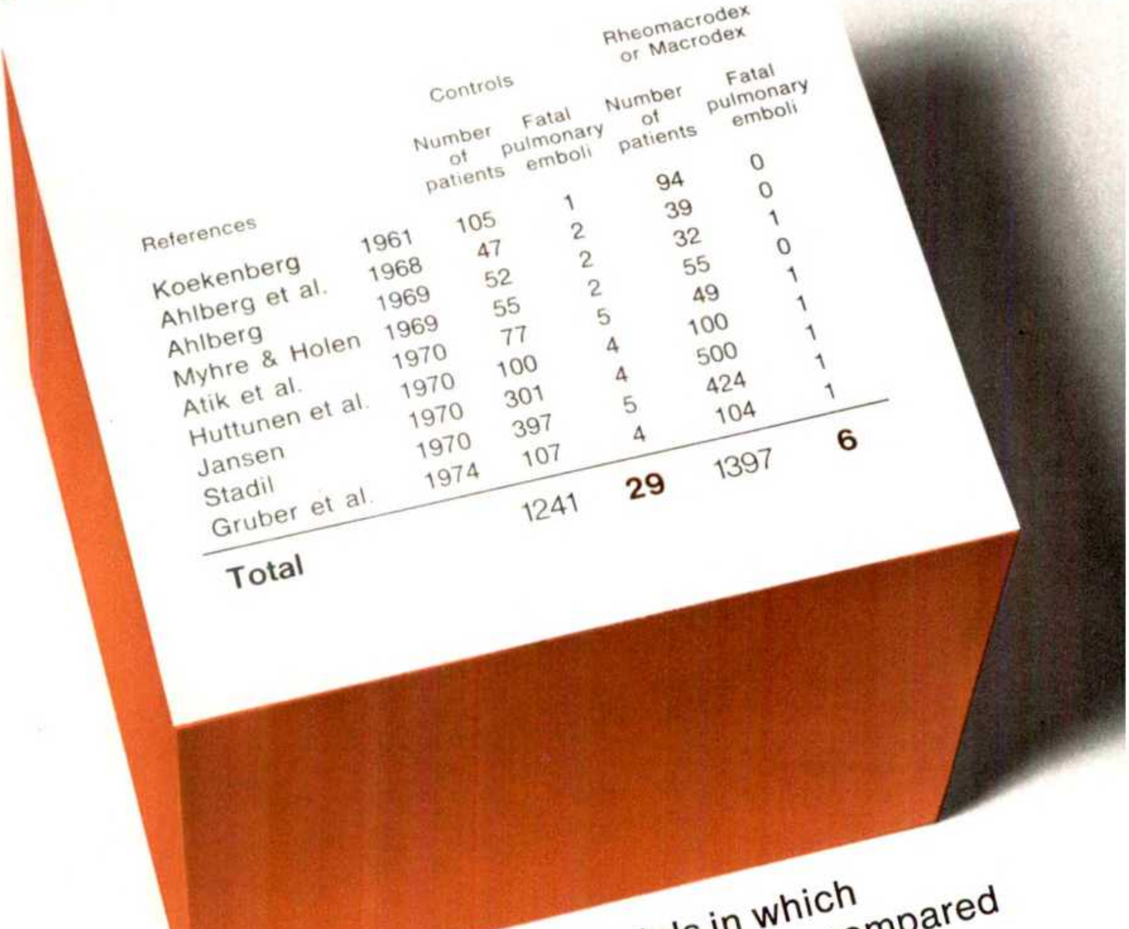
the need for post-operative blood transfusion
clot retention
catheterization
the risk of infection
the period of hospitalization

Presentation
Epsikapron Solution for Injection 0.4 g/ml Box of 6 ampoules of 10 ml, each containing 4.0g aminocaproic acid (0022/5003) Epsikapron Effervescent Powder 50% Box of 30 sachets, each containing 3.0g aminocaproic acid (0022/5004) Epsikapron Syrup 0.3g/ml Bottle of 250ml (0022/5005)

EPSIKAPRON®

Manufacturer: AB Kabi, Stockholm, Sweden.
Further information from:
KabiVitrum Ltd
Bilton House, Uxbridge Road, Ealing, London W5 2TH.
Telephone: 01-567 4717 or 01-579 1871.

Compelling evidence mounts up: Rheomacrodex and Macrodex reduce mortality from post-operative pulmonary embolism!



References		Controls Number of patients	Controls Fatal pulmonary emboli	Rheomacrodex or Macrodex Number of patients	Rheomacrodex or Macrodex Fatal pulmonary emboli
Koekenberg	1961	105	1	94	0
Ahlberg et al.	1968	47	2	39	0
Ahlberg	1969	52	2	32	1
Myhre & Holen	1969	55	2	55	0
Atik et al.	1970	77	5	49	1
Huttunen et al.	1970	100	4	100	1
Jansen	1970	301	4	500	1
Stadil	1970	397	5	424	1
Gruber et al.	1974	107	4	104	1
Total		1241	**29**	1397	**6**

Combined results of all trials in which Rheomacrodex or Macrodex were compared to controls and in which fatal pulmonary emboli were verified by autopsy.

Pharmacia

Pharmacia (Great Britain) Limited,
Paramount House,
75 Uxbridge Road,
London W5 5SS

Rheomacrodex and Macrodex comply with the dextran 40 and 70 BP 1973 monographs respectively.

Br. J. Surg. Vol. 62 (1975) 409–412

The surgical management of ingrowing toenail

W. R. MURRAY AND B. S. BEDI*

SUMMARY

A retrospective review has been carried out on 200 randomly selected patients with ingrowing toenail in order to assess the surgical management and its results. There was a predominance of males between the ages of 11 and 30 with an ingrowing toenail. Despite the high recurrence rate following simple avulsion of the toenail, its place in the initial management of the condition is justified. As regards more definitive surgery, total proximal nail bed ablation was found to give the best results. Sepsis at the time of operation neither increased the recurrence rate nor caused severe postoperative sepsis.

A surgical management policy for the treatment of ingrowing toenail is outlined and discussed.

AN ingrowing toenail complicated by pain and sepsis is a common condition often treated by chiropodists, general practitioners and casualty surgeons before being referred for a definitive treatment. The surgical treatment of this condition and the decision as to which form of treatment should be instituted are commonly left to relatively inexperienced junior surgical staff, who would welcome a clear-cut management policy. Unfortunately, this does not appear to exist for ingrowing toenails.

Lloyd-Davies and Brill (1963) showed that conservative outpatient management gave good results. However, their policy requires a careful and time-consuming follow-up by both the medical and nursing staff, combined with a high degree of patient co-operation.

The aims of the present study were therefore first to review the management and success of treatment of patients with a diagnosis of ingrowing toenail seen at the Western Infirmary, Glasgow, and secondly to construct a workable management policy, which could be applied to all such cases in the future.

Patients

The case records of 200 patients with ingrowing toenails between 1966 and 1970 were randomly selected and reviewed retrospectively. Patients with a diagnosis of onychogryphosis were excluded from the survey.

The surgical procedures used and reviewed in this survey were as follows:

1. Simple avulsion of the toenail.
2. Wedge resection of the medial or lateral aspects of the proximal nail bed as described by Winograd (1929).
3. Wedge resection of both medial and lateral aspects of the proximal nail bed by the technique of Winograd (1929).
4. Total proximal nail bed ablation as described by Zadik (1950).

Results

Epidemiology

The survey showed that the condition of ingrowing toenail affects males (68·5 per cent) more commonly than females (31·5 per cent). Males in the second and third decades of life accounted for 56 per cent of the patients in this series, the male predominance continuing into the fourth decade after which the incidence of ingrowing toenail is similar for both sexes (*Fig.* 1). Of the 200 patients in this study, 143 patients had only one hallux affected, and in 138 patients the condition involved both lateral and medial nail folds concurrently. In the remaining 62 cases where only one nail fold was affected at presentation it was more commonly the lateral fold than the medial fold (*Table I*).

Table I: DETAILS OF PATIENTS WITH INGROWING TOENAILS

	Patients	
Site of disease	No.	%
Single hallux	143	71·5
Both halluces	57	28·5
Both nail folds	138	69·0
Lateral fold only	43	21·5
Medial fold only	19	9·5

Table II: RESULTS OF SIMPLE AVULSION OF THE TOENAIL AT THE SAME SITE

No. of avulsions at the same site	Patients		Recurrence rate (%)
	No.	%	
1	95	65·5	64
2	35	24·1	86
3	15	10·4	80

Simple avulsion

One hundred and forty-five patients (72·5 per cent) had been submitted to at least one simple avulsion of the toenail, 70 per cent of these procedures being performed under a local anaesthetic and 30 per cent under a general anaesthetic. *Table II* shows that 65·5 per cent of the patients who had avulsion of the toenail had only one avulsion, 24·1 per cent had two avulsions at the same site and 10·4 per cent had more than two avulsions at the same site.

The recurrence rates of ingrowing toenails requiring further surgery in this group were 64 per cent following the first avulsion, 86 per cent following the second avulsion and 80 per cent after more than two avulsions.

---

* Department of Surgery, Western Infirmary, Glasgow.

Nail bed ablation

One hundred and fifty-eight patients (79 per cent) in this series sooner or later had some form of nail bed ablation, 65 per cent of these having had a previous simple avulsion. Ninety-seven per cent of the nail bed ablation procedures were performed under a general anaesthetic and 3 per cent under a local anaesthetic.

Table III shows that the commonest operation used was total proximal nail bed ablation (60 per cent), with 35 per cent undergoing Winograd single wedge resection and 5 per cent having a Winograd double wedge resection. The recurrence rate or nail regrowth rate at the site of ablation was similar for total proximal nail bed ablation and single Winograd wedge resection at 27 per cent, but higher for Winograd double wedge resection at 50 per cent. When the patients who did not require a further surgical procedure are excluded, the symptomatic recurrence rate was found to be 16 per cent for total proximal nail bed ablation compared with 25 per cent for Winograd single wedge resection and 50 per cent for Winograd double wedge resection.

Table III: RESULTS OF NAIL BED ABLATION PROCEDURES

Surgical procedure	Patients No.	Patients %	Nail regrowth No.	Nail regrowth %	Further operation* No.	Further operation* %
Single wedge resection	56	35	15	27	14	25
Double wedge resection	8	5	4	50	4	50
Total proximal nail bed ablation	94	60	25	27	15	16

* Symptomatic recurrence rate.

Table IV: TREATMENT OF SYMPTOMATIC RECURRENCE FOLLOWING NAIL BED ABLATION PROCEDURES

	Initial procedure					
	SWR (56 patients)		DWR (8 patients)		TPNA (94 patients)	
	No.	%	No.	%	No.	%
Further operation required	14	25	4	50	15	16
Second procedure	3	9	1	3	29	88
Recurrence	0		0		10	34·5
Third procedure	0		0		9	
Recurrence	0		0		0	

SWR, Single wedge resection. DWR, Double wedge resection. TPNA, Total proximal nail bed ablation.

Of the 33 patients with symptomatic recurrence requiring further surgery, 88 per cent were submitted to a total proximal nail bed ablation, with a recurrence rate of 34·5 per cent (*Table IV*). Ninety per cent of these recurrences were submitted to further total proximal nail bed ablation following which there were no recurrences.

Sepsis

Forty-five per cent of patients admitted for treatment of their ingrowing toenails had sepsis of the nail folds recorded at admission. Of the 158 patients submitted to nail bed ablation procedures, 28 per cent had sepsis present at the time of surgery. The sepsis had no effect on the rate of recurrence of ingrowing toenail.

Discussion

The epidemiological findings in *Table I* and *Fig. 1* show that the sample studied was similar to previously reported groups of patients suffering from ingrowing toenails (Fowler, 1958; Lloyd-Davies and Brill, 1963; Townsend and Scott, 1966). The predominance of

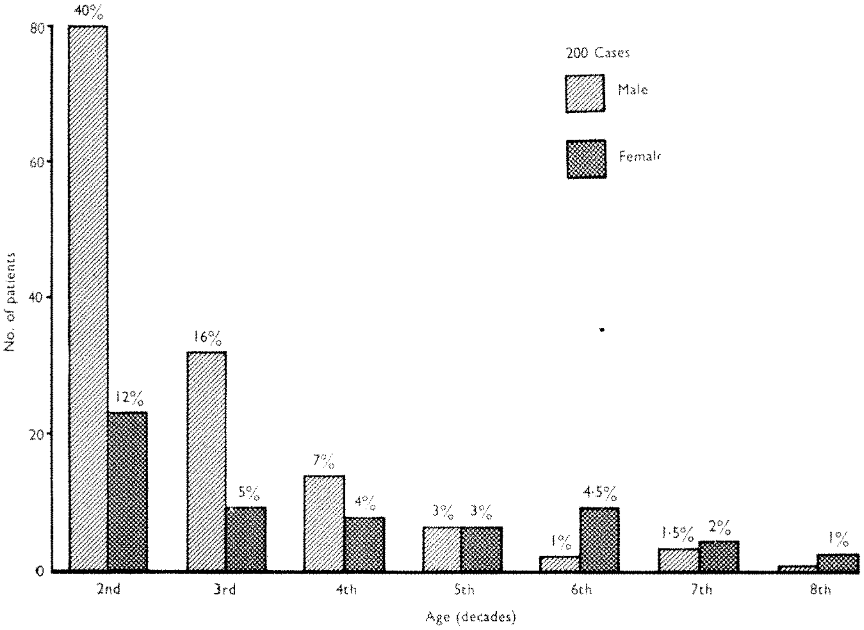


Fig. 1. Age and sex distribution of the patients with an ingrowing toenail.

males between the ages of 11 and 30 (56 per cent of patients) must be regarded as an important factor in planning a management policy. A painful ingrowing toenail which is inefficiently treated and requires numerous visits to hospital could well have a significant detrimental effect on education, career prospects and recreational activities in this group.

In this survey the recurrence rate of symptomatic ingrowing toenail following one avulsion was 64 per cent. However, cure is not the only aim of simple nail avulsion (Lloyd-Davies and Brill, 1963; Scott, 1968; Lepidus, 1972). The rapid relief of symptoms and the eradication of infection achieved by avulsion are important factors to be considered when contemplating the use of this treatment. For these reasons we feel that simple avulsion of the toenail has a definite place as a primary surgical procedure. Avulsion can easily be carried out on an outpatient basis under a local anaesthetic, unless infection has spread proximal to the interphalangeal joint, when a general anaesthetic should be used.

The importance of explaining to the patient simple conservative care of the new nail as it grows has been stressed elsewhere, and a follow-up clinic visit at 6 months to assess the success of the treatment is advised (Lloyd-Davies and Brill, 1963). If the condition has recurred and is causing symptoms, then more definitive surgery is called for. Our results show that the recurrence rate after a second avulsion at the same site was 80 per cent and is so high that further avulsion alone has little to offer. Some form of nail bed ablation should therefore be advised. A second avulsion is only indicated to eradicate a persistent and severe infection and to relieve symptoms prior to a more definitive procedure in the next few weeks. It is very difficult to justify more than two simple avulsions at the same site.

In this survey the commonest and most successful nail bed ablation procedure employed was total proximal nail bed ablation (Zadik, 1950), with a symptomatic recurrence rate of 16 per cent. This relatively high rate of recurrence is probably due in part to the lack of technical expertise of the junior surgical staff.

Winograd single wedge resection gave a higher symptomatic recurrence rate of 25 per cent, but may nevertheless be justifiable when performed properly in patients whose symptoms and signs have always been localized to one nail fold and who are loath to forfeit the whole of the nail. The results of Winograd double wedge resection suggest that this procedure should be abandoned in favour of total proximal nail bed ablation, although a large number of cases would be needed to confirm this impression.

Ninety-seven per cent of the nail bed ablations were performed under a general anaesthetic. This is a remarkably high figure when one considers that the anaesthesia for these procedures need be no greater than for a simple avulsion of a toenail, which is commonly performed under local anaesthesia. The use of local anaesthesia, sepsis permitting, allows satisfactory nail bed ablations to be carried out at an outpatient theatre session or on a day case basis, with minimal inconvenience to the patient and significant saving of the anaesthetist's time.

Fifty-five patients in our series were subjected to nail bed ablation without a previous avulsion of the toenail. It could be argued from our figures that approximately 20 of these patients would have regrown a normal nail if simple avulsion had been carried out as the initial surgical procedure.

In cases of troublesome recurrence following any of the ablation procedures, a total proximal nail bed ablation was commonly performed (88 per cent of patients), with a recurrence rate of 34·5 per cent. Townsend and Scott (1966) have stated that repetition of total proximal nail bed ablation for recurrence often proves unsatisfactory and recommend the use of the Symes terminal amputation procedure as reported by Thomson and Terwilliger (1951), and found satisfactory by Rees (1964).

Our results indicate that sepsis present at the time of a nail bed ablation procedure does not lead to an increased incidence of recurrence, as suggested by Townsend and Scott (1966). Moreover, the incidence of postoperative sepsis in our cases was surprisingly low and on no occasion was infection difficult to eradicate. The practice of performing a second avulsion on a recurrent septic ingrowing toenail 2–3 weeks before nail bed ablation, thereby rendering the nail bed clean, is, however, preferable to operating on a septic toe. This avulsion can be performed at the 6-month clinic visit or at a re-referral clinic visit and therefore does not unduly prolong the definitive surgery.

The outline of our management policy for cases of ingrowing toenail referred to the surgical clinic is now as follows:

1. Simple avulsion under local anaesthetic if there has been no previous surgical treatment.
2. Advice regarding conservative management of the new nail plus a 6-month clinic visit for assessment of the new nail growth.
3. Nail bed ablation under a local anaesthetic is advised for recurrent ingrowing toenails.
4. Septic recurrent ingrowing toenails are avulsed under local anaesthetic if possible and definitive surgery postponed for 2–3 weeks.

The use of this policy as a broad outline should result in the majority of cases of ingrowing toenail referred to surgical clinics being treated with minimal delay and inconvenience to the patient. A greater awareness by the junior surgical staff of the problems involved in the treatment of this annoying condition may well lead to improved management in the future.

References

FOWLER A. W. (1958) Excision of the germinal matrix: a unified treatment for embedded toe-nail and onychogryphosis. *Br. J. Surg.* **45**, 382–387.

LEPIDUS P. (1972) The ingrown toenail. *Bull. Hosp. Joint Dis.* **33**, 181–192.

LLOYD-DAVIES R. W. and BRILL G. C. (1963) The aetiology and out-patient management of ingrowing toe-nails. *Br. J. Surg.* **50**, 592–597.

REES R. W. M. (1964) Radical surgery for embedded or deformed great toe-nails. *Proc. R. Soc. Med.* **57**, 355–356.

SCOTT P. R. (1968) Ingrown toenails. *Med. J. Aust.* **1**, 47–51.

THOMPSON T. C. and TERWILLIGER C. (1951) The terminal Syme operation for ingrowing toe-nail. *Surg. Clin. North Am.* **31**, 575–584.

TOWNSEND A. C. and SCOTT R. R. (1966) Ingrowing toe-nail and onychogryphosis. *J. Bone Joint Surg.* (*Br.*) **48**, 354–358.

WINOGRAD A. M. (1929) A modification in the technique of operation for ingrown toe-nail. *JAMA* **92**, 229–230.

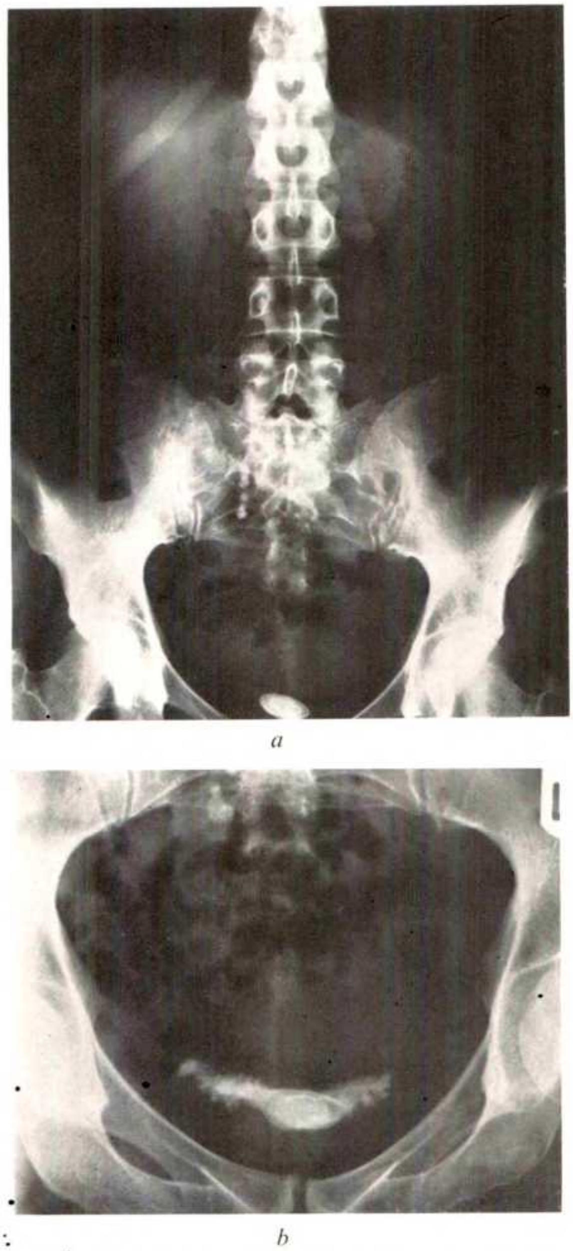
ZADIK F. R. (1950) Obliteration of the nailbed of the great toe without shortening the terminal phalanx. *J. Bone Joint Surg.* (*Br.*) **32**, 66–67.

Br. J. Surg. Vol. 62 (1975) 413–414

Hanging bladder stone formed around Mersilene mesh

P. P. DONGAONKAR*

FORMATION of a vesical calculus around a foreign body in the bladder is a well-known condition. Levack (1955) reported 2 cases of hanging bladder stones formed on unabsorbable suture and ligature. Weston (1957) reported another case of a similar nature. Chute (1962) published details of 8 cases of bladder calculi found around the fragments of ruptured Foley catheter balloons. Kiryabwire (1969) published a similar case of stone formation around a foreign body. Asopa (1965) described a case of formation of stone around a portion of stem of a plant, and Sood (1970) described the formation of a stone around a hair-pin; both of these foreign bodies were introduced into the bladder per urethra. A case is presented in which a bladder stone formed around a Mersilene mesh.


a

b

Fig. 1. *a*, Straight X-ray of the abdomen showing a calculus in the region of the bladder. *b*, Postmicturition intravenous pyelogram showing a calculus in the bladder.

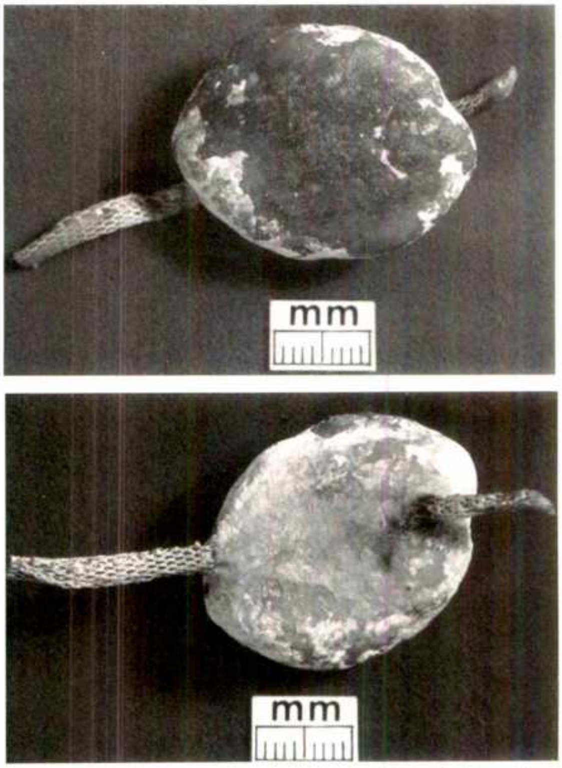


Fig. 2. Calculus showing incorporation of Mersilene mesh.

Case report

The patient, a 43-year-old married woman, presented at the Surgical Outpatients' Clinic, Rotherham Hospital, in 1974 with a history of urinary discomfort and haematuria on two occasions. She had had frequency of micturition for 2 years. In 1971 a urethral sling had been inserted for stress incontinence and the material used was Mersilene mesh. The stress incontinence had improved for a few months, but frequency and dysuria had continued.

---

* Rotherham Hospital, Yorkshire.

Straight X-ray of the abdomen and an intravenous pyelogram were performed which showed a large calculus in the bladder (*Fig.* 1). Both kidneys were functioning normally. Cystoscopy was performed and this confirmed the presence of a bladder stone. Suprapubic cystostomy was undertaken on 25 February 1974. It became apparent that there was a bladder stone which was hanging from the anterior wall of the bladder by two Mersilene slings. The stone was removed along with the Mersilene slings (*Fig.* 2). The patient's postoperative course was uneventful.

Conclusion

Mersilene mesh is being widely used for sling operations, but this would appear to be the first recorded case in the literature of the formation of a stone around Mersilene mesh protruding into the bladder.

Acknowledgements

I am grateful for the help and advice of Mr C. C. Rigby, Consultant Surgeon, Rotherham Hospital, and Mr D. Ballantine, Consultant Gynaecologist, Moorgate General Hospital, Rotherham, and for permitting me to report their patient.

References

ASOPA H. S. (1965) Foreign body vesical calculus in the male. *Indian J. Surg.* **27**, 724–726.

CHUTE R. (1962) Bladder calculi formed around retained fragments of ruptured Foley catheter balloons. *J. Urol.* **87**, 355–358.

KIRYABWIRE J. W. M. (1969) Vesical stone due to a foreign body. *East Afr. Med. J.* **46**, 371–375.

LEVACK J. H. (1955) Hanging bladder stone formed on unabsorbable suture and ligature. *Br. J. Urol.* **27**, 239–341.

SOOD S. (1970) Foreign body calculus in urinary bladder with hydronephrosis. *J. Indian Med. Assoc.* **55**, 19–20.

WESTON B. E. (1957) Hanging bladder stones. *Br. J. Urol.* **29**, 146.

Br. J. Surg. Vol. 62 (1975) 415–420

Reviews and notices of books

Orthopaedic Surgery

Edward L. Compere, California. 210×145 mm. Pp. 323, with 90 illustrations. 1974. London: Lloyd-Luke. £12·15.

THE title is misleading; this is essentially a handbook of operative surgery. The operations that the author has employed in his own practice are described, but many that are part of the standard orthopaedic repertoire are omitted. This policy seriously impairs the usefulness of the handbook. For many orthopaedic disabilities a number of operations are available and the selection of the correct procedure requires careful judgement. A trainee surgeon will look in vain for this information and will find the description of some of the techniques inadequate, though this is remedied to some degree by the numerous illustrations.

The reviewer is at odds with a number of statements. In anterior arthrodesis of the cervical spine, the trachea, oesophagus and thyroid gland are retracted medially, not laterally. A medial meniscectomy, as here described, becomes a major attack on the knee joint, which is not necessary for the average bucket handle tear.

The final chapter on 'Errors and safeguards in orthopaedic surgery' contains both good and bad advice. Volkmann's contracture is usually caused by an arterial injury and not venous stasis, and the release of tight dressings and plaster may not be adequate. A surgeon who follows the instructions in the paragraph on 'Amputation and the certainty of the diagnosis or malignancy' may be tempted to delay amputation for a malignant tumour because of equivocal radiographic appearances or the absence of severe pain, when the histological diagnosis is not in doubt.

R. BARNES

Bonney's Gynaecological Surgery

Edited John Howkings, London, and Sir John Stallworthy, London. Eighth edition. 234×155 mm. Pp. 868+x, with 507 illustrations. 1974. London: Baillière Tindall. £11.

PREVIOUS editions of this textbook on operative gynaecology have been regarded internationally as major reference works. Undoubtedly Bonney must be recognized as one of the great men of surgery, and perhaps the one who contributed most to the development of techniques of gynaecological surgery. The editors in their preface regard this eighth edition as 'possibly the final tribute of two pupils to their master, Victor Bonney', and certainly this edition lives up to its past reputation and indeed shows valuable innovations.

Despite quite drastic revision, some original text from previous editions, including the opening chapter on general operative considerations, can be found and many of the illustrations are still Bonney's originals. Human frailties in the editorial process creep into the best-organized volumes, and the reviewer found this no exception when, by chance, he discovered the interchange of captions between Figs. 145 and 146.

It is ten years since the last edition and this new volume reflects well the changes in thought and practice over this period. A good example of the revision is the chapter on 'The radical abdominal operation for carcinoma of the cervix' which now contains a very full account of the use and results of radiotherapy in association with surgery.

The last three chapters of the seventh edition have been dropped (blood transfusion, water and electrolytes in gynaecological surgery, radiotherapy of gynaecological conditions) and one chapter (31) now replaces two separate chapters on post-operative complications—general. The new chapter on 'Post-operative complications: cardiovascular system' is more or less unchanged in the first part but then goes on to include an excellent contribution on thrombo-embolism written by John Bonnar.

As indicated, revision has been extensive—even the reference to 'catgut blisters' has been updated! Newer techniques such as laparoscopy and vacuum curettage receive mention, and the personal interests of one of the editors in medical defence can be detected in reference to medicolegal aspects in at least one chapter.

This is an excellent book and must still be one of the best works on gynaecological surgery in the world. Certainly it should be available in the surgeons' rooms of general surgical and gynaecological departments alike, where it will surely give information, advice and possibly comfort to the surgeons faced by an unexpected gynaecological emergency.

D. V. I. FAIRWEATHER

Practical Surgical Management

A. M. C. Macgregor, Florida. Second edition. 180×120 mm. Pp. 150+ix. 1974. Edinburgh: Churchill Livingstone. £1·50.

THIS little book is full of useful information and fits snugly into a white coat pocket. These are two essential requirements for a book designed for house surgeons.

The arrangement is logical and the first chapter on 'Pre-operative management' consists largely of check-lists of investigations that may be required. 'Organisation of theatre' follows and is brief and to the point. 'Post-operative management' is dealt with next and again is composed of lists of such things as when to remove drains, drips, sutures and indications of recovery or complications, etc. 'Fluid and electrolyte management' followed by 'Intensive care' complete the section dealing with the care associated with operation. Another very brief chapter, this time dealing with 'Administration' is followed by one entitled 'Data'. The data referred to are a collection of normal values for haematology, blood and urinary chemistry, CSF and various other tests. All this information is useful, mainly accurate and helpful if some of the qualifications necessary to interpret this kind of information are remembered. Finally there is a chapter on 'Drugs' which is by no means complete but a useful starting point nevertheless.

The main point of such a book as this is to provide a framework around which the idiosyncrasies peculiar to a particular job can be built. With this point in mind perhaps a little spare space consisting of a few blank pages for notes and jottings would be helpful. Perhaps also in the next edition a note about SI units might be included, but with these two suggestions made, the book is recommended as a good buy for the house surgeon at the beginning of his job.

C. WASTELL

Transfusion of Blood Preserved by Freezing

S. Sumida, Fukuoka, Japan. 255×180 mm. Pp. 92+xiv, with 117 illustrations. 1974. Stuttgart: Georg Thieme Verlag. DM.58.

THIS elegantly produced monograph is an account of how Dr Sumida organized the first frozen blood bank in Japan. Inspired by an address given by that singular pioneer, Dr Charles Huggins of Boston, at a meeting of the Japan Society for Blood Transfusion in 1965, Dr Sumida lost no time in visiting Massachusetts General Hospital where he acquired the necessary skills and knowledge to set up a replica of the Huggins system for handling frozen cells for transfusion in Fukuoka.

For anyone wishing to follow his example, here is an explicit step-by-step description of the method, illustrated with excellent photographs and simple diagrams. The author has reappraised each step of the procedure by his own laboratory and clinical investigations, and a particularly interesting chapter is devoted to original observations on the changing morphology of red and white blood cells under the cryomicroscope.

While much of the technical section is concerned with the Huggins system which requires a high concentration of glycerol as the protective agent, a slow rate of freezing and mechanical refrigeration of the product at −80 °C, the author does give his more limited experience of the low glycerol rapid-freezing technique in liquid nitrogen at −150 °C. The parameters used to judge the quality of the final blood product, such as red cell recovery, post-transfusion survival, ATP content of red cells, etc., all favour the liquid nitrogen technique.

Apart from a single chapter dealing with the clinical advantages and disadvantages of frozen/thawed red cells, the book is mainly of interest to the technically minded. In the United Kingdom clinicians tend to leave decisions on methodology in blood banking to their colleagues in the National Blood Transfusion Service, and, in this sense, the decisions have already been taken as the five centres in this country now operating frozen blood banks have opted for the liquid nitrogen technique based on Krijnen's method, with local variations.

A chapter on techniques for freezing platelets is stimulating, but it is clear that the final choice of protective agent is still undecided and that the yield of viable platelets after freezing is disappointing.

W. J. JENKINS

The Treatment of Breast Cancer

Edited Sir Hedley Atkins. 210 × 145 mm. Pp. 222. 1974. Lancaster: Medical and Technical Publishing Company. £7·50.

AN introduction to this volume states: 'The aim is to attempt to bridge the gap between standard textbooks and research papers and to provide an assessment of the various methods available'; in this it succeeds admirably. The authors, each a recognized authority on a particular aspect of breast cancer, review the evidence to support prevailing attitudes to the disease, and interest is maintained by leaving the reader to draw his own conclusions on the presented evidence.

A recurring theme in the text is the need for reappraisal of many theories in relation to breast cancer, which through repetition and long usage have come to be accepted as facts on which many of our principles for the management of the disease are founded. The reader's attention is repeatedly drawn to the urgent need for identification of the biological factors which constitute host resistance to the disease. The authors deal with surgical treatment, radiotherapy, endocrine therapy, chemotherapy and finally with tests of prediction in relation to breast cancer.

From a personal viewpoint, the reviewer found the chapter on tests of prediction particularly stimulating and a challenge to the future. In the present state of our knowledge it is accepted as necessary to put the salient evidence in front of the reader, but in this particular field one must leave its interpretation to experts on the subject, such as the author and his colleagues. Whilst concentrating mainly on endocrine status in relation to breast cancer, the author concedes that other factors such as viral infection and immune response may be equally important.

This volume is to be recommended for every ward library as a reasoned guide to the problem of breast cancer at this time. It highlights the need for combined effort in diagnosis and treatment in a field which is no longer the sole province of the surgeon and radiotherapist. It will be of particular interest to all oncologists and it is hoped that future editions of this book will maintain the excellence of the first.

JAMES F. PHILIP

Diagnosis and Early Management of Trauma Emergencies. A Manual for the Emergency Service

Edited Robert J. Touloukian and Thomas J. Krizek. 230 × 150 mm. Pp. 149 + vii, with 23 illustrations. 1974. Springfield, Ill.: Charles C. Thomas. $10.75 cloth. $6.75 paper.

EVERY doctor working in an accident and emergency department needs a guidebook; something like an instruction manual, concise, factual, lucid and didactic. The present book aims at just this target; it achieves a near miss. Brevity has been achieved by restricting the discussion to trauma; most British casualty officers (the book is manifestly transatlantic) will regret this limitation even though the title has warned them to expect it.

There are only three chapters. The first is wide-ranging and fascinating; in 19 pages it touches on triage, responsibility, medicolegal liability and even security. The second deals with ambulatory problems including open wounds, battered babies (? ambulatory), hand infections, maxillofacial trauma and eye injuries. The third and longest chapter deals with life-threatening emergencies: the obstructed airway, shock, head, chest and abdominal injuries, as well as fractures and dislocations.

Much of the guidance (apart from a cursory and actively misleading account of the care of the injured hand) is sound, but access to the information is sometimes difficult. The authors clearly try to achieve a systematic approach and often succeed, but when the going gets rough they sometimes lose heart. The line drawings are striking and useful, but extraordinarily inelegant.

This book needs to be re-edited, with the chapters and headings rearranged and in a format designed to fit a white coat pocket. Only then will the authors' single-minded concentration on the early management of the injured patient, their sound and sensible approach to severe injuries and their interesting views on organization gain proper recognition and enjoy widespread application.

A. GRAHAM APLEY

Clinical Neuro-surgery

Congress of Neurological Surgeons, Volume 21, Honolulu, Hawaii, 1973. 228 × 150 mm. Pp. 387 + xv. Illustrated. 1974. Baltimore: Williams & Wilkins. $19.50.

THIS book reports the annual meeting of the Congress of Neurological Surgeons. This society is unusual in several respects; its office bearers are all comparatively young (by statute) and its meetings are specifically planned as an educational exercise. Consequently, this annual publication is eagerly awaited and seldom disappoints. As is the usual style, this volume has several papers on each of a limited number of topics. Surgery of the pituitary, aneurysm surgery and the management of pain are this year's foci of interest. Each chapter is long enough to develop its theme satisfactorily, as well as to illustrate it, and has adequate references. Most describe the author's personal experience and attitude to the topic under discussion, and it is useful to read advocates of alternative techniques in succeeding chapters. There are two review articles, on the immunological and on the viral aspects of brain tumours—a reminder that whilst so much effort has gone into stereotaxic surgery and the management of aneurysms in the past two decades there has been little progress in the management of tumours. This volume should be of interest to many other surgeons, in view of the discussions on pain and on endocrine aspects of pituitary surgery.

BRYAN JENNETT

Chirurgie der Gegenwart

Edited R. Zenker, München, F. Deucher, Aarau, and W. Schink, Köln. 260 × 180 mm. Vols 4 and 5, pp. 22, 47, 50 and 35. Illustrated. 1974. München: Urban & Schwarzenberg. No price given.

FOUR further chapters have now been published. These include a detailed discussion of metabolic changes in the skeleton and the various disease processes which reflect upon skeletal changes. Three other chapters are related to orthopaedics. These cover injuries to the central nervous system in relation to vertebral damage, the management of pseudo-arthroses and finally the management of fractures of the lower limb. The chapter on pseudo-arthroses contains numerous rather horrifying illustrations but the writers do point out the mistakes made at the time of initial treatment and in relation to the causation of a failure to unite. The emphasis in the chapter on fractures of the tibia and the femur is definitely on the operative side and conservative management gets little mention.

It is unfortunate that the chapters of this multi-volume work are being numbered in relation to their time of publication so that the final numbering may appear rather irrational. However, this is obviously going to be a reference book rather than one to be read from cover to cover, so that the detailed numbering may not matter so much.

H. B. ECKSTEIN

The Myocardium: Failure and Infarction

Edited E. Braunwald, MD, Boston, with the collaboration of Amy Selwyn, Hospital Practice. 280 × 210 mm. Pp. 409 + xviii. with 350 illustrations. 1974. Reading: W. H. Freeman and Company. £10·40.

THIS is a most unusual book because the chapters originally appeared as individual papers in *Hospital Practice*. The authors are an extremely distinguished group and all of them have revived and modernized their articles for this volume. The coverage is broad, section I dealing with cardiac contraction mechanisms from ultrastructure through biochemistry, calcium metabolism and the biochemical basis of heart failure. Section II deals with physiological mechanisms of heart failure, with Dr Braunwald himself contributing a chapter on the autonomic nervous system in heart failure. Sections follow on the clinical manifestations of heart failure in adults and children, in heart muscle disease and in cor pulmonale. The treatment of heart failure follows. Section V gets down to the meat of the book and deals very fully with atherosclerosis and the mechanisms of myocardial infarction. It starts with the development of the atherosclerotic plaque and goes through primary prevention in children, the role of platelets and thrombosis, the pathology of the coronary arteries in fatal ischaemic heart disease, the genetic aspects of hyperlipidaemia and, finally, aggressive behaviour as a risk factor. The next section deals with what follows myocardial infarction: the biochemical and morphological changes, the haemodynamic consequences and sudden death. Section VII deals with treatment from the coronary care unit through anti-arrhythmic drugs, the management of arrhythmias, the present status of anti-thrombotic therapy and protection of the ischaemic myocardium. The surgical aspects are not forgotten and we find a chapter on myocardial revascularization from the Cleveland Clinic and the recognition and surgical treatment of imminent infarction. Mechanical assistance of the failing circulation and surgical myocardial revascularization during post-infarction shock conclude the surgical aspects of coronary artery disease. Finally, rehabilitation is not forgotten.

Dr Braunwald and his collaborator Amy Selwyn have done a splendid job of integration between the different authors' contributions and there is abundant cross-referencing to the material in other chapters when this is closely related. Dr Braunwald and his team are to be congratulated on achieving such remarkable balance and cohesion between the different chapters. The illustrations also are of a uniform excellence and are printed in a pleasing duo-tone which adds to their clarity. There are no references at the ends of the chapters. Selected reference sources for each chapter are collected together at the end of the book.

This book is highly recommended for covering the topic which it sets out to treat in such a readable and informative way and it will be of interest to both general physicians and cardiologists as well as to cardiac surgeons wishing to extend their vision beyond the operating table and to all students of the heart and circulation. Its price at £10·40 is not excessive for these days.

C. M. OAKLEY

Vascular Malformations (Angiodysplasias)

Edited E. Malan, Milan. 240 × 170 mm. Pp. 213, with 176 illustrations. 1974. Milan: Carlo Erba Foundation. No price given.

PROFESSOR MALAN edits this review of his experience of vascular malformations which must be unique. He is assisted by eighteen contributors, mostly his colleagues in Parma and Milan. He has collected the amazing number of 451 vascular malformations which, in most surgeons' experience, are relatively rare. The clinical aspects are comprehensively described and the illustrations are beautifully depicted. This is a monumental work, an accumulation of clinical experience over many years. There is a most useful chapter on malformations affecting the head and neck. This will no doubt be accepted as the definitive work on the presentation and treatment of vascular malformations. Anyone seeing and treating these conditions must consult this work. The bibliography is comprehensive and invaluable.

Minor criticisms must be made but in no way detract from the overall worth of this monograph. The classification is cumbersome, difficult to absorb and difficult to remember. The chapter on aetiology is unconvincing and does not show any advance over the past 25 years. It is still not possible to say where the shunts are sited in cases of diffuse arteriovenous communications. There is no mention of the use of ultrasound in the investigation of arteriovenous shunting. It is disappointing that Professor Malan is disenchanted with his imaginative operation of 'deafferentriation', that is, extensive division of arterial branches in cases of diffuse congenital arteriovenous anastomoses. Lastly, a small point, but the binding is poor and came apart during the reviewer's reading of the book.

L. T. COTTON

Atlas of Hand Surgery

Robert A. Chase, MD, California. 310 × 240 mm. Pp. 438 + xi. Illustrated. 1973. London: W. B. Saunders Company. £12·75.

THIS *Atlas of Hand Surgery* by Robert A. Chase is a well-illustrated and comprehensive volume. It covers all aspects of hand surgery from trauma to the elective surgery of such conditions as rheumatoid arthritis, Dupuytren's contracture and the reconstructive surgery of irreparable nerve lesions. The descriptive text is well amplified by clear diagrams and photographs. It reflects current opinion but unfortunately does not include a bibliography or list of references. Nevertheless, as the author states, 'the material presented in this atlas is based on case experiences'.

This book offers sound practical advice, and as such should prove a useful addition to a hospital library. For those concerned with the day-to-day management of problems of hand surgery it will be most valuable.

DONAL BROOKS

Emergency Abdominal Surgery, in Infancy, Childhood and Adult Life

Peter F. Jones, Aberdeen. 240 × 165 mm. Pp. 808 + xx. Illustrated. 1974. Oxford: Blackwell Scientific Publications. £13·50.

THE first objective of the author of this excellent book was to give the trainee surgeon a background knowledge of the whole field of emergency abdominal surgery. The second was to provide a handbook for consultation on specific problems and detailed advice on management and technique. Both objectives have been achieved with most unusual success. Writing with the confidence and competence based on his experience of emergency surgery over the past quarter of a century, Mr Jones has described the methods he has used and their advantages and disadvantages with refreshing candour and objectivity. Of course, no other surgeon will agree with all he says, but no one can doubt that the advice he gives is sound and comprehensive for those for whom he has written, and is often better than can be found in other books of this kind. In the sense that she is said to have inflicted every one of her recipes on her own family, this book could fairly and in no unkindly way be called the 'Mrs Beeton' of modern emergency abdominal surgery and is unhesitatingly recommended to the surgical maiden of today. The whole subject is covered including pre- and postoperative treatment and emergencies in the newborn, infancy and childhood. The chapters on acute appendicitis and intestinal obstruction are particularly good, and there are very helpful sections on the acute abdomen in pregnancy and the puerperium, gynaecological disorders, medical causes of acute abdominal symptoms and urological emergencies.

There are good and very helpful line drawings of the details of many operative techniques and interesting historical notes, and the references to the important original accounts of diseases and operations will be of much value to the young surgeons for whom this book is primarily written.

This book can be recommended most strongly to the surgeon in training, especially those who for whatever reason lack supervision, and to any surgeon who has to deal with the acute abdominal emergency. It should be in every hospital library for those who cannot afford their own copy.

A. W. WILKINSON

Handbook of Psychiatry

Edited Philip Solomon, San Diego, and Vernon D. Patch, Boston. Third edition. 210 × 135 mm. Pp. 706. 1974. Los Altos, California: Lange Medical Publications. $8.

THIS is the third edition of a comprehensive handbook of psychiatry that manages to compress a vast amount of information into a little over 700 small pages. There are forty short didactic chapters by a large number of authors who succeed in covering most topics in a thorough and eclectic manner, although of necessity in a book of this size covering so much there can be comparatively little discussion of many controversial issues. One has the impression that in the attempt to get completeness of coverage, some authors are not writing from their own experience but quoting from not always accurately remembered student textbooks. The brief notes on some aspects of epilepsy, for example, do not fairly cover the somewhat complex problems that many such patients have. Likewise, although there is a short interesting note on the dynamics of the surgeon–patient relationship, there is nothing on the psychiatric aspects of pain, which are certainly of interest to the surgeon. One of the new chapters is on transcultural psychiatry, and this seems to fall into the common fault of assuming that a foreign or immigrant patient will necessarily have specific and subtle problems which cannot be assessed by orthodox methods. No reference is made to many of the current epidemiological studies in different countries; for example, of schizophrenia by the WHO. Of necessity, the administrative and legal aspects of psychiatry entirely reflect the American scene.

Medical students in this country will thus find this book of only limited value, though it is certainly better than most of the short texts that are popular in this country. Most chapters have quite lengthy references which, if the student has time to read some of them, might act as a useful check against the didactic approach of the main text. The relative absence of references in comparable British books is to be deplored as it tends to discourage the student from reading more widely on his own account.

D. A. POND

Surgical Pathology

Lauren V. Ackerman, New York and St Louis, and Juan Rosai, St Louis. Fifth edition. 260 × 200 mm. Pp. 1394+xii, with 1392 illustrations. 1974. London: Henry Kimpton. £21·60.

THERE are some books that rapidly establish themselves as definitive texts. Ackerman's *Surgical Pathology* is such a work. When it first appeared in 1953 it was obvious that this was not yet another book written about surgical aspects of pathology ('the pathology of the living' as Dr Ackerman neatly calls it). Instead, here was the subject looked at, and described, by someone who was actually working in the surgical pathology laboratory, and who knew the problems faced by both surgeon and pathologist in diagnosis. This book is an invaluable aid to anyone with such a problem; its place is on the bench (next to the cut-up area and the microscope) rather than in the library or in a bookcase.

Having said that, it is still very readable with a lively style and sense of humour; for example, in the description of the indications for frozen section where, having emphasized that the technique is only indicated if it affects treatment then and there, the authors state that it should not be used 'to satisfy the surgeon's intellectual curiosity, or to prove that the pathologist is in the hospital'.

The present edition maintains the previous high standards and the references are up to date (and quote from the current British and American literature, which is not always the case with North American books). The major areas of pathology are covered with the exception of the ear; and, because biopsies from this site are such a common diagnostic problem, it seems worth while to suggest that the next edition includes a small chapter on aural pathology. Wisely, there are no plates in colour, but the black and white photographs and photomicrographs are very clear. It would, however, be helpful to have an indication of the actual size of gross specimens (e.g. Fig. 855, p. 854 is described as 'large', but no scale is included). These are but minor matters in a work to which everyone concerned with surgical pathology must refer.

P. M. SUTTON

Surgical Treatment of Facial Injuries

V. H. Kazanjian and J. M. Converse, New York. Third edition. 252 × 175 mm. Pp. 1482+xxxiii. Illustrated. 1974. Baltimore: Williams & Wilkins. £30.

A SCIENTIFIC treatise that reaches its third edition in twenty years under the baton of the original authors is a tribute both to them and to the value of the work itself. So it is with the *Surgical Treatment of Facial Injuries*, already established as a classic, and which now is a record of 75 years' combined personal experience of Dr Kazanjian and Dr Converse.

It might seem strange that an apparently small section of surgery requires 1500 pages in two volumes fully to account for all its activities but it does. The early chapters deal with basic principles of the processes of healing, the art and craft of facial surgery, as well as a tribute to anaesthesia. There follows an important dissertation on the emergency management of facial injury, a subject which perhaps should be better understood in casualty departments. The complexities of facial fractures are dealt with in some 200 pages and the details of many techniques of immobilization are described and well illustrated. As is to be expected the dental aspects of jaw fractures are clearly and carefully outlined.

A consideration of facial injuries in childhood serves to introduce the reader to the problems of facial growth and to the late effects of injury. One aspect of this subject which might have warranted a mention is the effect of irradiation on the young face, not only upon the soft tissues but upon skeletal development.

A section on radiography of facial bones contributed by Dr J. Zizmor presents the essential outlines of this diagnostic technique. It includes a discussion on pantomography which is now an invaluable adjunct to the study of skeletal and dental aberrations. There follow six chapters on general principles of reconstructive surgery in which is condensed the fundamental theory and techniques of tissue transplantation. All graftable tissues are discussed and there is a useful section on skin transplantation using the pedicle flap methods and their application to facial surgery. The remainder of the text deals with the correction of established facial deformities which follow trauma. These are set out on an anatomical basis and are as complete a record of the subject as will be found anywhere.

The various conditions are amply illustrated with line drawings and with photographs from the authors' vast library and many cases of special interest are to be found.

For the young surgeon here is a book which may be read from cover to cover with interest and without boredom. For the established practitioner here is an essential part of his armamentarium to which he will undoubtedly refer until the advent of the fourth edition which in due time will surely appear.

J. N. BARRON

Dupuytren's Disease

Edited J. T. Hueston and R. Tubiana. 275 × 210 mm. Pp. 167. Illustrated. 1974. Edinburgh: Churchill Livingstone. £7.

THIS monograph under the joint Editorship of John Hueston and Raoul Tubiana is based on the 1966 SICOT papers presented in Paris and subsequently produced by the Group d'Etude de la Main in French. This is the first English edition but is not simply an English translation of the previous French publication. This edition has been greatly expanded by contributions from well-known authorities on the subject and by revision of the earlier texts. The result is a fascinating narrative starting with a thumbnail sketch of the Baron himself and thereafter including all aspects of the disease and its treatment.

There is certainly no more authoritative work on the subject in the English language and it is doubtful whether in the years to come it will be superseded. Each contributor has added something of worth or exposed some new facet of 'this mysterious disease'. Although it is almost a century and a quarter since Dupuytren described a condition which he believed to be primarily an affection of the palmar fascia it seems strange that, while the treatment has been clarified over the years, the aetiology still remains obscure.

This is a splendid monograph, immaculately produced and illustrated and one that those who are concerned with the surgery of the hand will wish to have in their library.

DONAL BROOKS

The Practical Management of Head Injuries

John M. Potter. Third edition. 184×125 mm. Pp. 98+xiv, with 8 illustrations. 1974. London: Lloyd-Luke. £2.

THE appearance of the third edition of Mr Potter's well-known and valuable little book is to be warmly welcomed, not only by the 'casualty officers, orthopaedic and general surgeons, general practitioners and senior nurses' for whom, as the introduction states, it is primarily intended, but also by many teachers of surgery, who, like the reviewer, have sought to recommend the book to undergraduates but have been dismayed to find the book out of print for far too long.

Since the first edition appeared in 1961 there have been a number of imitators (at least two from Australasia) who have published a 'slim volume' concerning the management of head injuries, but none has quite achieved the readability or the comprehensiveness that Mr Potter has provided within the space of 98 pages of text.

There is an introduction, four chapters, three short appendices and a good index. The chapters deal, in logical sequence, with management in the casualty department and in the ward, with complications and lastly with convalescence, rehabilitation and sequelae. The information given is precise and clear at every stage and above all is entirely practical and to the point.

Rightly, no attempt has been made to involve the reader in theoretical conceptions nor is the underlying pathology described in any detail, basic knowledge being assumed. Similarly, special aids to diagnosis such as the EEG, angiography, isotope scanning, etc., have been eschewed because, in the circumstances for which the book is primarily conceived, specialist advice and assistance may not be promptly available. However, as a minor point of criticism, times are changing and in many accident departments in the United Kingdom and elsewhere some or all of these aids are becoming better understood and increasingly utilized. Echo-encephalography is, nevertheless, mentioned, albeit with deserved reservations. Perhaps it is too much to hope that by the time the next edition appears the EMI scanner will have resolved some at least of our diagnostic difficulties in this field!

BERNARD HARRIES

1974 Year Book of Plastic and Reconstructive Surgery

Edited Kathryn Lyle Stephenson et al. 194×130 mm. Pp. 360, with 127 illustrations. 1974. London: Lloyd-Luke. £12·50.

IT might be thought that the quick and easy way of keeping up to date in a speciality is to purchase the Year Book dealing with your subject. An expensive method perhaps. In the present volume over 200 papers are reviewed (up to July 1973) under regional anatomical groupings—the head, neck and thorax, genitalia, limbs, with further sections on burns, shock, anaesthesia, wound healing, neoplasms and transplantation—a wide variety of topics. For the busy surgeon the book offers much, but makes difficult reading because so often the abstract is not a true precis of the published paper but a short extract. Even the 127 figures fail to clarify poorly written texts.

Many of the 200 publications relate to retrospective surveys which have little place today unless the conclusions can point the direction in which a proper clinical trial should be made, indicating new observations to be followed or present new concepts. In some papers the author has muddled actual numbers and percentages, a feature which the editors (all seven of them) should have corrected; often because the numbers were small the use of percentages give completely false impressions. Editorial comments follow many of the extracts but, in the reviewer's opinion, could be more detailed (what is the 'Lipshutz technic'?) and more telling. A short authoritative essay preceding each section would help to put into perspective the extracts that follow. Indeed, the problem of selection of papers for presentation in this form has not been solved by this issue, especially when one considers that techniques are reported which are well known and well documented in standard textbooks.

This compact and nicely bound volume can be recommended for the busy man who does not subscribe to journals or who has little time to read them.

JAMES CALNAN

The Physiology of the Joints. Volume 3. The Trunk and the Vertebral Column

I. A. Kapandji, Paris. Second edition. 275×220 mm. Pp. 251, with 397 illustrations. 1974. Edinburgh: Churchill Livingstone. £4.

THIS is an important publication. As Professor Merle D'Aubigne writes in his preface to the French edition, it 'is a dedicated work by Dr. Kapandji, the artist and teacher, who has not only imagination and a flair for mechanics, but also the ability to communicate his ideas in a precise and simple fashion'.

Although it may be trite to recall that anatomy may be the handmaiden of the surgeon, there is a danger that the systematic and topographic anatomy learnt on the cadaver may blind us to important aspects of the anatomy of function, in particular the biomechanics of muscle and joint activity in life.

This volume is the third of a series on the physiology of joints and deals with the trunk and vertebral column; the first dealt with the upper limb and the second with the lower limb. These volumes are in their second edition translated from the French. It is impossible to summarize the wealth of information and it is recommended most highly, in spite of the trifling irritation caused by the translator's occasional lapses, in particular the excessive use of the definite article, correct in the original French but irritating to an English reader.

Nevertheless, the message is crystal-clear and those interested in biomechanical problems will deepen their understanding as to how groups of muscles work in patterns as prime movers, antagonists or synergists.

As an illustrator of original ideas the author can have few medical peers.

L. KESSEL

Fluid, Electrolyte and Nutrient Therapy in Surgery

Edward E. Mason, MD, PhD, Iowa. 234 × 155 mm. Pp. 352+vi, with 55 illustrations. 1974. London: Henry Kimpton. £5·95.

THIS book emphasizes the surgeon's responsibility to have a clear understanding of the metabolic changes in his patients at all times. This is virtually a single author work by a practising surgeon with the exception of the last chapter. The aim of the book is to enable surgeons to handle metabolic problems more effectively.

The style at times becomes anecdotal and it is difficult to follow the reasons for including various sections in a book of this nature, as on occasions the reader is led into bypaths which are in themselves quite interesting.

The first section naturally deals with body composition and its measurement. Subjects such as fluid and electrolyte balance are covered adequately and in considerable detail. The section on nutrition, however, is somewhat limited. Many recent developments in amino-acid preparations for parenteral use are not dealt with, and there is no mention of the role of intravenous fat as an important calorie source in intravenous feeding programmes. Some of the problems of parenteral feeding are identified clearly.

There is a detailed chapter on intestinal bypass surgery for obesity which also contains an interesting diversion on the aetiology of recurrent peptic ulceration after gastric surgery.

The section on calcium and phosphorous metabolism goes far beyond the title of the volume and contains a detailed discussion of the diagnosis of primary hyperparathyroidism, the differential diagnosis of hypercalcaemia and the surgical management of primary hyperparathyroidism. This is a good chapter, but it is odd that this subject should be dealt with in such detail when fluid and electrolyte problems associated with other endocrine tumours are barely mentioned.

The style and presentation of this book preclude its use as an intensive care manual. It is unlikely that it will be used to seek help with specific problems as it is only in the last chapter that clear recommendations for definite problems are set out in any detail. However, this is an interesting, quite detailed book on a very important subject and could be a useful source book for postgraduate students reading in the overall field of fluid electrolyte and nutrient therapy.

IVAN D. A. JOHNSTON

Reviews and notices of books

The Genetics of Locomotive Disorders

C. O. Carter, London, and T. J. Fairbank, Cambridge. 160× 240 mm. Pp. 170+xii. 1974. London: Oxford University Press. £5.

THIS book is concerned with the inheritance of various diseases of bone, muscle, joints, nervous system and connective tissues. Most of the text is devoted to bone disorders, localized abnormalities of the limbs and syndromes involving the skeleton. The style is clear with a short section for each disease which includes a brief clinical description, the genetic information and the appropriate references at the end. It is not a textbook of diagnosis. There are no illustrations and only a few tables which deal with the analysis of genetic data. It is a reference book for those who, having diagnosed a particular disease, wish to know about the mode of inheritance. So much is acknowledged by the authors in their preface so the absence of clinical illustrations is not surprising. However, some comparative tables would have been useful for highlighting important clinical or genetic differences between rather similar diseases. This book will be most useful to clinical geneticists, orthopaedic surgeons, paediatricians and physicians interested in bone disease. There is not sufficient in it about joints to interest the rheumatologist and the genetics of connective tissue disorders is covered by McKusick in his very comprehensive monograph on that subject. Neurologists and neurosurgeons may prefer the earlier Oxford monograph which deals entirely with the inherited diseases of nerve and muscle. It is unlikely that a general surgeon would refer to it very often, but it will be a quick, easy and authoritative reference book for those with special interests in bone disorders and skeletal malformations.

D. P. BRENTON

Review of Medical Pharmacology

Frederick H. Meyers, San Francisco, Ernest Jawetz, San Francisco, and Alan Goldfien, San Francisco. Fourth edition. 260×180 mm. Pp. 721. Illustrated. 1974. Los Altos, California: Lange Medical Publications. No price given.

THIS is an eminently readable, though humourless, textbook. It is liberally illustrated with clear diagrams indicating drug structures and pharmacological concepts. Conventionally organized in sections it deals in different sections with drugs acting on different systems of the body, with chemotherapeutic agents, etc. None of the sections is unduly long, the aim being to present concise useful information. Accordingly, only one or two drugs having a particular action are discussed—this is a deliberate policy to avoid bewildering the student with lists of tranquillizers, antibiotics, etc. Each chapter ends with a short list of key references, so the information in the text could readily be expanded by the interested reader.

If the book has a fault it lies not so much with the authors as with the FDA, who so restrict the use of new drugs in the United States that the authors are forced to admit that propranolol is not approved for use in essential hypertension or in hyperthyroidism, and that bethanidine and clonidine are not available in the United States. This, naturally, reduces the reader's confidence in the personal experience of the authors.

Although the fourth edition appeared in 1974 it still does not contain any reference to such recent advances as the invention of drugs which block histamine H_2-receptors or the discovery that aspirin blocks prostaglandin synthesis, but these are minor points.

The book as a whole is a most valuable text.

J. H. WYLLIE

The Cutting Edge. Early History of the Surgeons of London

R. Theodore Beck, Surrey. 235×165 mm. Pp. 214+xvi. Illustrated. 1974. London: Lund Humphries Publishers. £6.

THIS book will appeal not only to the medical profession but also to the lay public, for it provides a fascinating and very interesting insight into the early history of healing.

The author, a well-known architect, has the right background to write such a book as this, for he is a past master of the Worshipful Company of Barbers, a life member of the Royal Archaeological Institute, Fellow of the Society of Antiquaries, Fellow of the Royal Society of Arts, Fellow of the Royal Institute of British Architects and a member of the Court of Common Council of the City of London. Theodore Beck, when Sheriff of London in 1969 was invited by the President and Council of the Royal College of Surgeons to give the Thomas Vicary lecture.

A laudatory foreword to this book is written by The Lord Mayor of London, Lord Mais, during his reign of office in 1973.

The early history of the barber-surgeons concerns the City of London to a great extent, and also the surgery of the battlefield during the Hundred Years' War. The author has vividly portrayed the extent of surgical operations during this period. Throughout the book the illustrations are of a high order and have been well chosen.

The traditional *Fair Book of Surgery* compiled by Thomas Morstede, the most eminent surgeon of the fifteenth century, was thought for centuries to have been lost but has been found and identified by the author in the Harleian Collection in the British Museum. It was written in 1446 and extensive extracts from this ancient book are quoted.

The series of events which led to the union of the Guild of Surgeons and the Barbers Company to form the Barber Surgeons Company in 1540 are well presented.

Perhaps one of the most useful parts of this book is the inclusion of biographical notes at the end of each chapter; these will be of real value to medical historians of the future. A concluding chapter describes the life and times of Thomas Vicary, Sergeant Surgeon to King Henry VIII, and his contemporaries. Theodore Beck should be warmly congratulated on writing this book, for he has added considerably to our knowledge of the early history of British Surgery.

CECIL WAKELEY

The Treatment of Prostatic Hypertrophy and Neoplasia

Edited J. E. Castro. 210×145 mm. Pp. 200+xii. Illustrated. 1974. Lancaster: Medical and Technical Publishing Company. £6·75.

ALTHOUGH numerous books have appeared on the various techniques of prostatic surgery, there has not been an attempt to collate all aspects into one small volume until now. In many ways this book represents a new, very readable and extremely up-to-date account of all that is known about the prostate, starting with an excellent summary of the biology and the pathological changes in both the benign and malignant glands. It is rare for the pros and cons of controversial therapeutic methods to be presented in successive chapters so clearly and so concisely.

An excellent description of the surgery of the benign hypertrophy of the prostate, including a full bibliography, leaves the future prostatectomist fully conversant with the various methods open to him.

Crysosurgery, a new method, is described in detail, listing the advantages and disadvantages of this rather novel form of therapy, and there is an excellent chapter on the conservative medical treatment by a contributor from the United States.

The whole subject of neoplasia is fully ventilated, an aspect which at the present time of re-evaluation of conventional methods of treatment, is extremely valuable. The radical surgical approach, the conservative approach and the various hormonal methods of control of the disseminated disease are explained clearly.

This volume merits careful reading by all scientists and clinicians who are interested in the recent observations and techniques of treatment of prostate disease. In the foreword the editor quotes Professor Huggins: '... more than half the male population over the age of 50 suffer from benign tumours of the prostate'. This alone should make this book essential reading for the majority of our profession.

DAVID WALLACE

Management of Surgical Complications, 3rd Edition

Edited by Curtis P. Artz, *Medical University of South Carolina,* and James D. Hardy, *University of Mississippi School of Medicine,*

Prevention is better than cure, so the expert contributors to this widely used work advise on the steps that might be taken to avoid complications—as well as offering plenty of helpful information if they do set in.

Approx 865pp (315 illus) Price £16.65 Hardback binding April 1975

Atlas of Vaginal Surgery

By Professor Gunther Reiffenstuhl, *Frauenklinik, Salzburg, Austria, and* Dr Werner Platzer, *Anatomischen Instituts der Universitat, Innsbruck, Austria.* Edited by Emanuel A. Friedman, *MD, Med. ScD., Beth Israel Hospital, Boston.*

A magnificent, two-part, atlas of gynaecologic surgery. The first section—*Anatomical Description*—by Platzer comprises 70 text pages and 42 drawings; the second—*Operative Technique*—by Reiffenstuhl has 300 pages of text and 330 illustrations.

Approx 600pp (370 illus—full colour throughout) Price £55.55 July 1975

Physical Examination of the Surgical Patient, 4th Edition

An Introduction to Clinical Surgery

By J. Engelbert Dunphy, *MD, University of California School of Medicine,* and Thomas W. Botsford, *MD, Harvard Medical School.*

This 4th edition of a best-selling text includes major changes in the elective examination of the heart, breast, abdomen, and the cancer patient; and the emergency examination of the chest and abdomen and the thermally injured patient.

Approx 430pp (215 illus, 2 in colour) Price £8.85 Hardback binding April 1975

For an inspection copy of these valuable texts write to Colin Dann, Publicity Manager, at 120 Golden Lane, London EC1Y 0TU, quoting ref. WBS 6.

W. B. Saunders Company Ltd
12 Dyott Street London WC1A 1DB

New Titles from

CHURCHILL LIVINGSTONE

THE ESSENTIALS OF CARDIOVASCULAR SURGERY

WILLIAM H. BAIN and J. KENNEDY WATT

1975 Second edition

160 pages illustrated £3·25

STRESS FRACTURES

MICHAEL DEVAS

1975 256 pages illustrated £15·00

CONCISE SURGERY OF THE ACUTE ABDOMEN

JOHN A. SHEPHERD

1975 210 pages illustrated £5·50

INTENSIVE CARE

Proceedings of the Eighth Pfizer Symposium

Edited by W. F. WALKER and D. E. M. TAYLOR

1975 260 pages illustrated £9·50

RECENT ADVANCES IN PAEDIATRIC SURGERY

Number Three

Edited by ANDREW W. WILKINSON

1975 230 pages illustrated £7·00

CHURCHILL LIVINGSTONE

23 Ravelston Terrace, Edinburgh EH4 3TL

The Principles of Transurethral Resection and Haemostasis

J. P. MITCHELL, T.D., M.S., F.R.C.S., F.R.C.S.E.

276pp. 124 illus. £6·00

Demonstrations of Physical Signs in Clinical Surgery 15th edition

HAMILTON BAILEY

Edited by A. CLAIN, M.B., F.R.C.S.

632pp. 996 illus. £7·50

Plastic and Reconstructive Surgery

HANS MAY, M.D., F.A.C.S.

1270pp. 916 illus. £27·35

(F. A. DAVIS) in slipcase.

Cardiac Surgery

Editor D. E. HARKEN, M.D.

No. 1 330pp. 86 illus. £5·70

No. 2 198pp. 38 figs. £5·70

(F. A. DAVIS)

Fundamentals of Cardiopulmonary Resuscitation

JAMES R. JUDE, M.D., and JAMES O. ELAM

162pp. 72 figs. £1·85

(F. A. DAVIS)

JOHN WRIGHT

42-44 Triangle West, Bristol BS8 1EX

H. K. Lewis & Co. Ltd.

Medical Publishers
and Booksellers

136 GOWER STREET
LONDON, WC1E 6BS

Telephone : 01-387 4282

Ready this month . . .
16th Edition of

BAILEY AND LOVE'S
SHORT PRACTICE
OF SURGERY

revised by A. J. HARDING RAINS
and H. DAVID RITCHIE
1308 pp. 1482 illustrations £10·00 net.

BURNS including Thermal Injury

The Journal of the International Society for Burn Injuries

Editor: J. E. LAING, FRCS

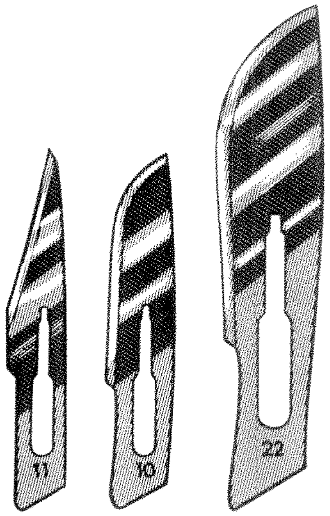
Published Quarterly Annual Subscription £8·50 (post free) Single Copies £2·40 (post free)

JOHN WRIGHT **42–44 Triangle West**
Bristol BS8 1EX

The operative word is

Swann-Morton

surgical blades



SWANN-MORTON LIMITED. PENN WORKS.
OWLERTON GREEN, SHEFFIELD S6 2BJ, ENGLAND.

Synopsis of Anaesthesia

7th Edition

J. ALFRED LEE, FFARCS, DAHon FFARCSI, *Honorary Consulting Anaesthetist to the Southend-on-Sea Hospital;* and R. S. ATKINSON, MA, MBBChir, FFARCS, *Consultant Anaesthetist, Department of Anaesthetics, Southend-on-Sea Hospital.*

'It is a true compendium of knowledge which will be read avidly by every examinee throughout the world. The authors deserve the highest praise for producing such a worthy volume.' *World Medicine*

1000 pages 31 illustrations £5·00 net.

Synopsis of Surgical Anatomy

11th Edition

D. J. Du PLESSIS, ChM(Rand), FRCS(Eng), *Head of Department of Surgery, University of the Witwatersrand, Johannesburg; Chief Surgeon, Johannesburg General Hospital.*

About 900 pages 779 illustrations £7·00 net.

The Choroid Plexus in Health and Disease

Edited by M. G. NETSKY, MD, *Professor of Neurosurgery, University of Virginia School of Medicine;* and S. SHUANGSHOTI, MD, *Assistant Professor of Pathology, Chulalongkorn University, Bangkok, Thailand.*

363 pages 195 illustrations £20·00 net.

Essentials of Urology

D. E. STURDY, MS, FRCS, *Surgeon, Royal Gwent Hospital, Newport, Mon.*

'The book will no doubt be read by many young people, because it is easy to read and it fills a gap in the urological shelves of hospital libraries.' *British Medical Journal*

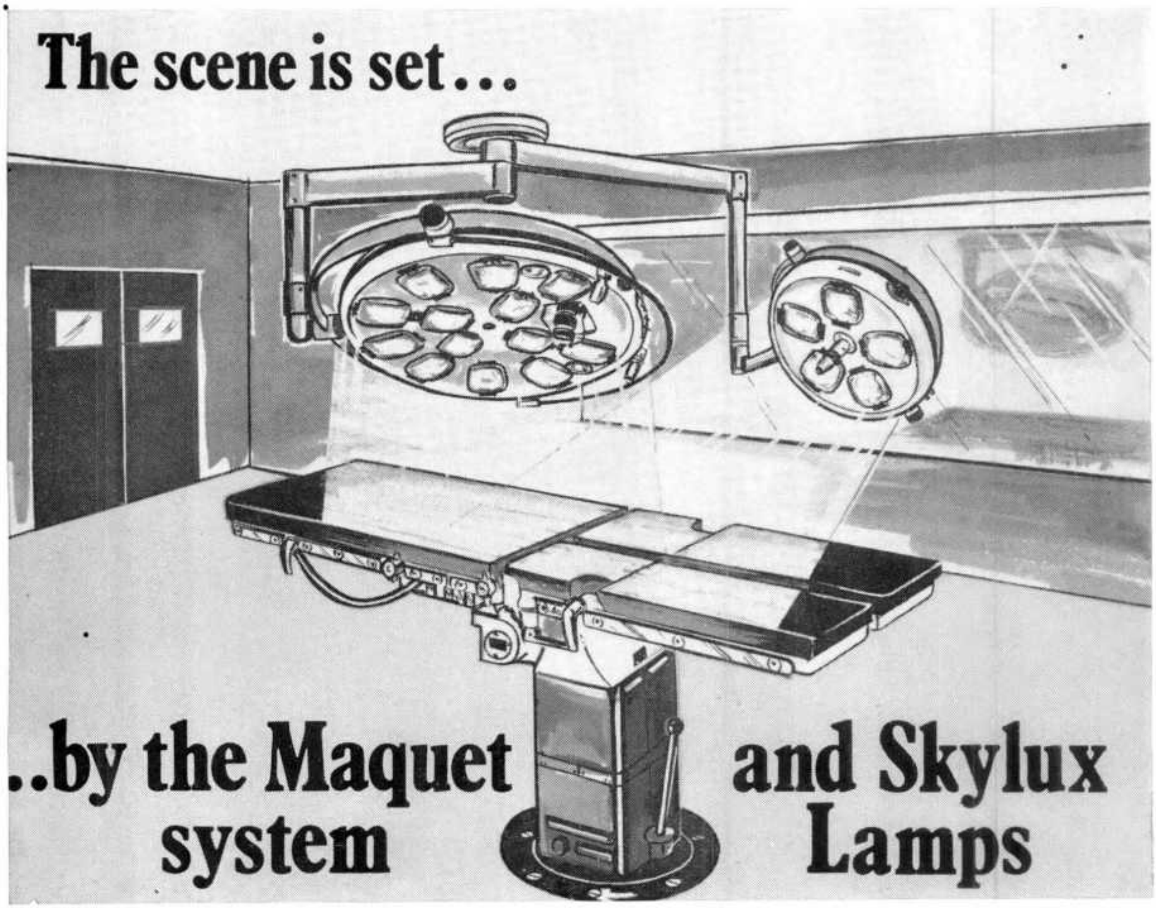
'This is a well-written, well-illustrated book, more than adequate for the undergraduate, valuable to the postgraduate.' *General Practice*

'This book fills a need, particularly for the medical student and the candidate for a general surgical postgraduate degree. . . . The line drawings are clear, and the radiographic reproductions are excellent and clearly illustrate the text.' *South African Medical Journal*

306 pages 215 illustrations £5·00 net.

JOHN WRIGHT

42–44 Triangle West, Bristol BS8 1EX



The scene is set...

..by the Maquet system and Skylux Lamps

Maquet fixed column operating table system

Fixed column–power operated

Extreme stability

Free access for x-ray equipment

Wide variety of table tops

Tops easily interchangeable–
increased theatre efficiency

Unique 'Tele' control

Easy clean finish

Skylux Lamps - for all Theatre applications

- High level of light intensity
- Maximum freedom from shadow and glare
- Ideal variation of illumination
- Heat free
- A real white light
- Easy mobility

Catalogues available on request

Downs Surgical Ltd

CHURCH PATH, MITCHAM, SURREY 01-648 6291

SIEMENS

DIATHERMY EQUIPMENT
for modern
ELECTRO-SURGICAL
TECHNIQUES

Available in various designs such as

TROLLEY MOUNTED,
CEILING SUSPENSION
or installation in the
OPERATING THEATRE WALL

Full details available on request

Sierex

SIEREX LIMITED Electro-Medical Department,
Heron House, 109 Wembley Hill Road,
Wembley HA9 8BZ Telephone 01 903 0418

Branches in Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester, Newcastle and Reading. Agents in Belfast.

GU

NEW

DIATHERMY
FORCEPS,
SCISSORS &
SCALPEL HANDLES
COVERED
WITH
LONG-LIFE..

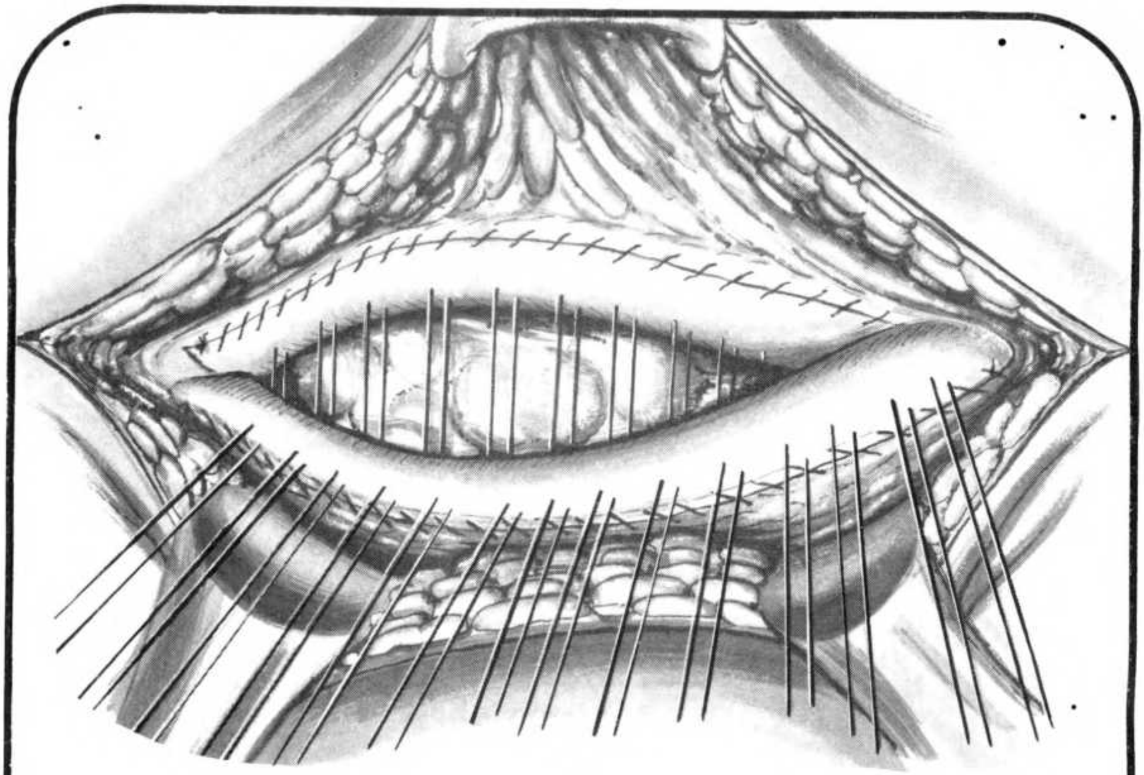
Insulast

- Developed for autoclaving
- ECONOMICAL · saves on repairs
- SAFER · crack resistant
- THINNER · better grip
- Universal cable fitting

When ordering new diathermy instruments, or requiring old instruments to be re-insulated, always specify 'INSULAST' only obtainable from;

The G.U. Manufacturing Co. Ltd.

28a, Devonshire Street, London, W1N 2AJ
Telephone; 01-935-2835.



Marlex Mesh...

now available in sterile packs!

Since its introduction in 1958 Marlex Mesh has developed into a highly successful item for Surgical reconstruction.
Marlex Mesh is an inert, knitted polypropylene mesh through which tissue grows easily forming a new, strong fibrous wall.

Available in a range of sizes individually packed and sterilised ready for use.

For full details please write to:–

The Marketing Manager,
Davol International Limited,
Freepost, Clacton, CO15 3BR, Essex.

(No stamp required if posted within U.K.)

DAVOL

Personal Patient Protection from Davol - leaders in Health Care for over 100 years

The single solution

for parenteral nutrition

Aminoplex 5

1 litre three times per day provides 15g. of utilisable nitrogen and 3000K calories; the nutrient content being derived from synthetic L-Form amino acids, sorbitol and alcohol.

Geistlich
Chester

In co-operation with Salvia-Werk G.m.b.H., Homburg/Saar, W.Germany.

Medical literature
available from:
Geistlich Sons Ltd.,
Newton Bank,
Long Lane,
Chester CH2 3QZ.
Telephone
Chester 47534-7

staphylocidalpenetrateability!

no other word
is big enough for
fucidin*

'This antibiotic has now established itself as an important antistaphylococcal agent in the treatment of systemic infection. Good absorption and minimal side effects after oral administration combined with an impressive penetration in deep-seated infections gives fucidin an important place in the management of staphylococcal infections.'

* fucidin is a trade mark for sodium fusidate

Further information available on request.

Leo Laboratories Limited,
Hayes Gate House, Hayes, Middx.

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU

Trasylol

significantly reduces mortality and morbidity in acute pancreatitis

Trapnell, J. E. *et al.* (1974) *British Journal of Surgery*, **61**, 177.

Trasylol®

(aprotinin)

Bayer

® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

Vol. 62 : No. 6 : June 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society)
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
I. D. A. JOHNSTON Newcastle
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN McADAM Kampala : Uganda
A. C. McEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX

Subscription £15 per annum, post free. Single copies £1·50, post free

---

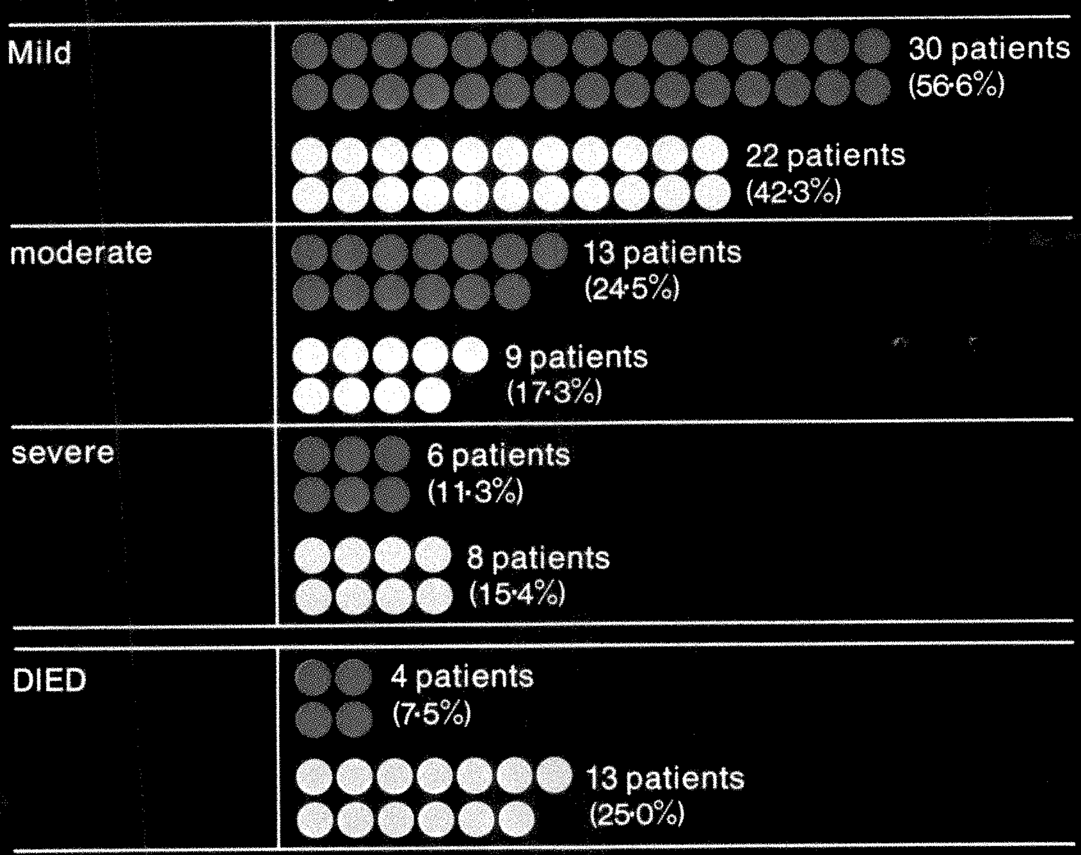
THE WILLIAMS & WILKINS CO., BALTIMORE

Subscription $36·00 per annum. Single copies $3·00

Second Class Postage paid at Baltimore, and at additional mailing offices.

The new evidence for Trasylol in the treatment of acute pancreatitis

Prospective double-blind trial in 105 patients over a five year period shows Trasylol to significantly reduce mortality and morbidity in acute pancreatitis.[1]



● Trasylol group (53)
○ placebo group (52)

'Trasylol must therefore be regarded as a drug which is beneficial in the treatment of acute pancreatitis.'[1]

[1] Trapnell, J.E. *et al.* (1974) *British Journal of Surgery*, **61**, 177

Trasylol®
(aprotinin)

Bayer
® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

The British Journal of Surgery

Vol. 62 : No. 6 : June 1975

Original papers

		Page
Hepatic resection	G. B. Ong and N. W. Lee	421
The effect of hepatic ischaemia on liver function and the restoration of liver mass after 70 per cent partial hepatectomy in the dog	R. J. Mackenzie, C. M. Furnival, Maureen A. O'Keane and L. H. Blumgart	431
Orthotopic liver transplantation utilizing a vascular stapling instrument	P. T. Barron, I. J. Vogelfanger and W. G. Waddell	438
Effect of surgical trauma on plasma concentrations of cyclic AMP and cortisol	G. V. Gill, K. Prudhoe, D. B. Cook and A. L. Latner	441
Early management of corrosive burns of the oesophagus	M. Balasegaram	444
The management of peptic oesophageal stricture	R. C. N. Williamson	448
The effect of raising the concentration of potassium in the blood or intestinal lumen on the trasnport of potassium in the dog intestine	Anne Hardy Smith and R. Shields	455
Environmental tests of linear flow ventilation for an operating theatre	The late Charles C. Scott and Thomas D. Guthrie	462
Bilateral idiopathic parotid duct strictures	M. Adiseshiah	468
General anaesthesia during early pregnancy	Leo Strunin, K. Knights, J. M. Strunin and Michael E. Ward	471
Renal transplantation in the unimmunosuppressed pig: an abnormal response	John Terblanche, Rosemary Hickman and C. J. Uys	474
Injuries caused by rubber bullets: a report on 90 patients	R. Millar, W. H. Rutherford, S. Johnston and V. J. Malhotra	480
Incidental appendicectomy with laparotomy for trauma	Lawrence W. Norton, Marna Sweeney and Ben Eiseman	487
A prospective study of acute pancreatitis	C. W. Imrie and A. S. Whyte	490
The use of the vas deferens in inguinal herniorrhaphy	Patrick Sames	495
Nitrogen mustard as adjunctive chemotherapy for breast carcinoma	James R. Hines and John S. Williams	497

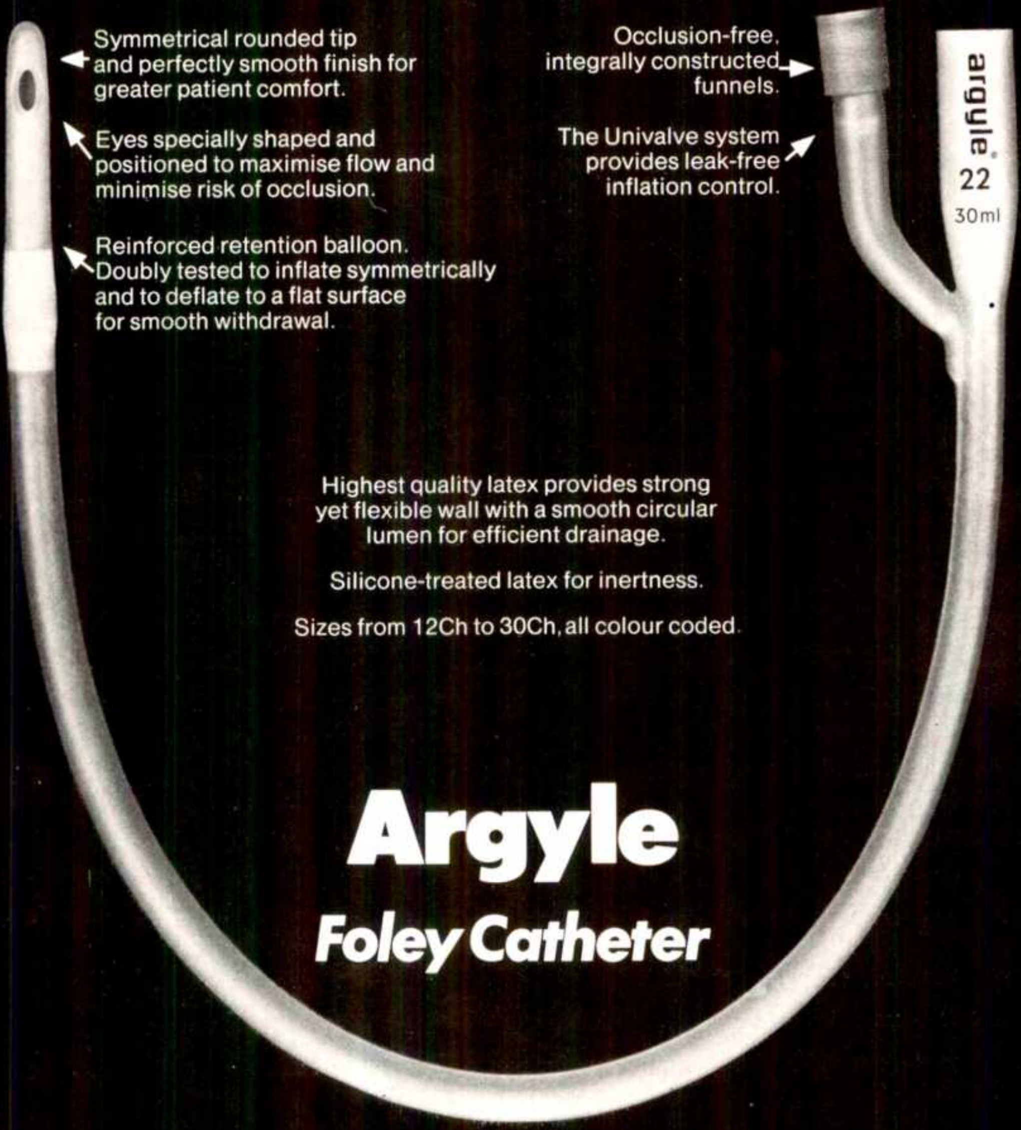
Reviews and notices of books 501

© John Wright & Sons Ltd and the respective contributors named above. 1975.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any other form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.

for Foley read Argyle

Read why the Argyle Foley Catheter is simpler, safer, surer than any other Foley catheter



Symmetrical rounded tip and perfectly smooth finish for greater patient comfort.

Eyes specially shaped and positioned to maximise flow and minimise risk of occlusion.

Reinforced retention balloon. Doubly tested to inflate symmetrically and to deflate to a flat surface for smooth withdrawal.

Occlusion-free, integrally constructed funnels.

The Univalve system provides leak-free inflation control.

Highest quality latex provides strong yet flexible wall with a smooth circular lumen for efficient drainage.

Silicone-treated latex for inertness.

Sizes from 12Ch to 30Ch, all colour coded.

Argyle
Foley Catheter

Sherwood
MEDICAL INDUSTRIES
Sherwood Medical Industries Limited,
London Road, County Oak, Crawley, West Sussex, RH10 2TL.
Telephone: Crawley (0293) 34501. Telegrams: Shermed Crawley. Telex: 87685.

CAT Nos 5ml Balloon MAR 4405, 30ml Balloon MAR 4430.

'Argyle' is a trade mark. 0044

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 60. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISEMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

PRESENTATION OF STATISTICS

Authors are reminded that with the frequent use of statistical analysis in biological writing of all kinds it is desirable that:

a. The methods section of a paper should contain a mention of any statistical technique used. If the method is new or unfamiliar either a reference should be given or a description included as a brief appendix.

b. If alternative techniques could have been applied to the data, a short justification of the method is often appropriate.

c. In clinical trials the confidence or tolerance limits of the results should be quoted, particularly when formal statistical significance at the 5 per cent level is only just reached.

d. Abbreviations for statistical terms should follow those used in *Documenta Geigy Scientific Tables*, 7th edition, 1970.

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are two or more authors (apart from the main author), these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated.

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature* (*Lond.*) **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea **4**, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva*. Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th 3d. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology*. London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BLAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

Congress Proceedings

CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding, or that following.

SAINSBURY P. (1955) *Suicide in London*. London, Chapman & Hall. (Maudsley Monograph No. 1.)

Compelling evidence mounts up: Rheomacrodex and Macrodex reduce mortality from post-operative pulmonary embolism!

References		Controls		Rheomacrodex or Macrodex	
		Number of patients	Fatal pulmonary emboli	Number of patients	Fatal pulmonary emboli
Koekenberg	1961	105	1	94	0
Ahlberg et al.	1968	47	2	39	0
Ahlberg	1969	52	2	32	1
Myhre & Holen	1969	55	2	55	0
Atik et al.	1970	77	5	49	1
Huttunen et al.	1970	100	4	100	1
Jansen	1970	301	4	500	1
Stadil	1970	397	5	424	1
Gruber et al.	1974	107	4	104	1
Total		1241	**29**	1397	**6**

Combined results of all trials in which Rheomacrodex or Macrodex were compared to controls and in which fatal pulmonary emboli were verified by autopsy.

Pharmacia

Pharmacia (Great Britain) Limited,
Paramount House,
75 Uxbridge Road,
London W5 5SS

Rheomacrodex and Macrodex comply with the dextran 40 and 70 BP 1973 monographs respectively.

Forthcoming Titles

AUGUST

Disaster Planning

Proceedings of a Symposium held at the Royal Naval Hospital, Haslar, Gosport, Hants.

Edited by Surgeon Commander J. W. RICHARDSON, OBE, FRCS, RN, *Consultant Surgeon, RN Hospital, Haslar.*

These papers, which have been presented by those people recognized as experts in their particular field, discuss many contentious points which underline the need for an agreed policy regarding the management of casualties arising from disaster situations. This book is a 'must' for all those concerned with the formulation of disaster plans: police, fire service, ambulance, doctors (accident surgeons, pathologists), hospital staff, voluntary service, coroners, the media. Those concerned with running nuclear power, industry, the railways, aircraft and ships and the sea.

144 pages　19 illustrations　paper covers　£5·00 net.

SEPTEMBER

Chest Injuries

G. KEEN, MS, FRCS, *Thoracic and Cardiac Surgeon, United Bristol Hospitals and Frenchay Group of Hospitals, Clinical Lecturer in Thoracic Surgery, University of Bristol.*

There are many pitfalls of diagnosis and treatment in chest injury that are responsible for avoidable complications and deaths. The book is based on the author's own experience. It will be useful to general surgeons, accident surgeons and anaesthetists and it will also be a practical guide for those who find themselves dealing with a case that is outside their experience.

192 pages　78 illustrations　about £8·00 net.

JOHN WRIGHT

42–44 Triangle West, Bristol BS8 1EX

ARMOUR TEMPORARY BIOLOGICAL DRESSING CAN SOLVE THE IMMEDIATE PROBLEM OF TISSUE LOSS COVERAGE AND REPAIR

effective in the treatment of

- partial thickness burns
- debrided full thickness burns
- traumatic skin loss injuries
- soft tissue defects
- decubitus and vascular ulcers

The many advantages of using a biological dressing are

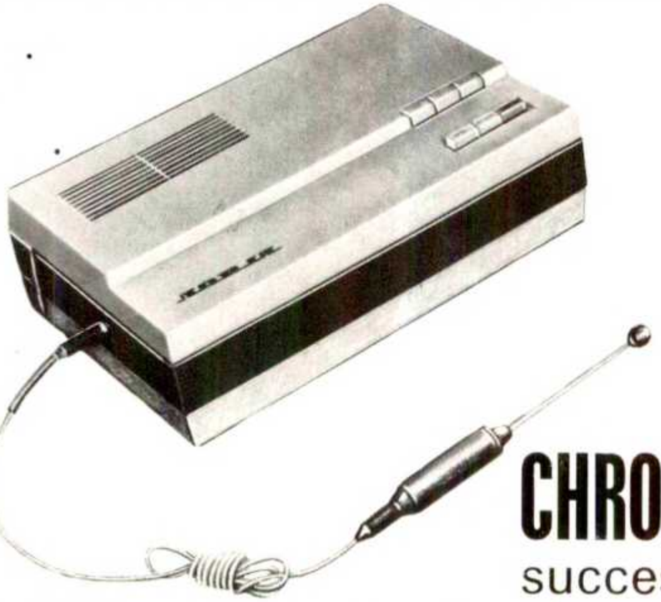
- dramatic reduction of pain
- reduction of fluid and protein loss
- reduction of heat and energy loss
- reduction of infection
- increase in mobility
- protection of exposed tendons, vessels and nerves
- promotion of healing
- psychological improvement of the patient
- improvement of scarring
- In full thickness burns, used as a "test material" to predict the readiness of the granulating bed to accept autograft. This results in a more economical use of autograft material.

Armour porcine skin dressings are presented in sterile lyophilised form, can be conveniently stored without refrigeration and may be reconstituted prior to use in sterile water or balanced electrolyte solution.

Package and size availability is as follows:
Boxes of 5 x 1 sq. ft. roll 3"x 48"
Boxes of 5 x ¼ sq. ft. roll 3"x 12"
Boxes of 10 Patches 2½"x 4"
Boxes of 5 x Wide Strip 8"x 18"
Boxes of 5 x Wide Half Strip 8"x 10"

Full product information on request from
Armour Pharmaceutical Company Limited
Eastbourne Sussex England BN22 9AG

JA6/ABD/5



The LOR-1A
APPARATUS

CHRONIC TONSILLITIS

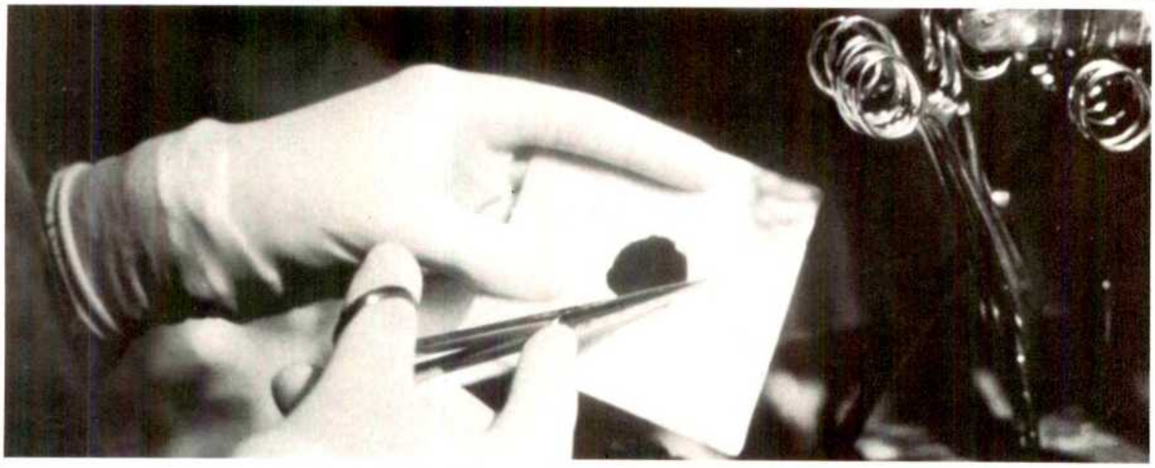
successfully treated by
ultrasonic therapy

The LOR-1A apparatus produces mechanical vibrations of ultrasonic frequency which have a therapeutic effect on infected tonsils. Clinical tests have shown 75% success in patients treated. Advantages of the LOR-1A are its small dimensions and low weight (less than 5 kg and its proven safety, reliability and ease of operation. Small ultrasonic generator of loss operating voltage permits direct treatment to tonsils.

Detailed information available from

V/O MEDEXPORT

31 Kakhovka, Moscow 113461, USSR. Telex 7247
Tel: 121–01–54



The first word in ostomy management

Skin care after ileostomy, colostomy or ileal conduit starts at the time of surgery itself. Stomahesive protects peristomal skin making the patient comfortable and more confident about his future.

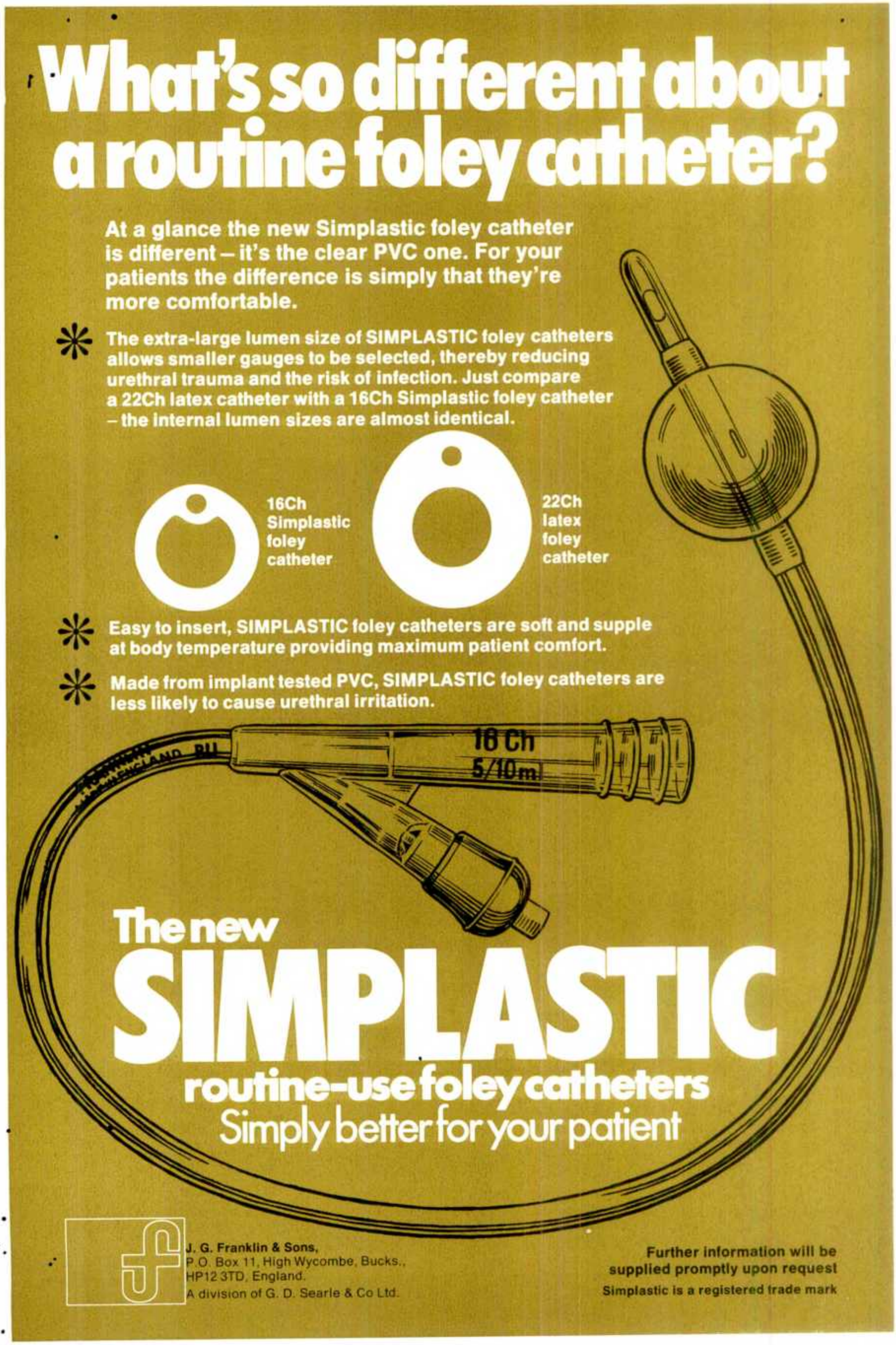
Because Stomahesive contains non-sensitising ingredients, it can be used even on broken, excoriated skin. But why wait for trouble?

Use Stomahesive - right from the start.

Stomahesive, available in boxes of 5 10cm × 10cm squares.

Stomahesive is a Squibb registered trademark. Full information available on request to E.R. Squibb and Sons Limited, Regal House, Twickenham TW1 3QT.

SQUIBB



What's so different about a routine foley catheter?

At a glance the new Simplastic foley catheter is different – it's the clear PVC one. For your patients the difference is simply that they're more comfortable.

✻ The extra-large lumen size of SIMPLASTIC foley catheters allows smaller gauges to be selected, thereby reducing urethral trauma and the risk of infection. Just compare a 22Ch latex catheter with a 16Ch Simplastic foley catheter – the internal lumen sizes are almost identical.

✻ Easy to insert, SIMPLASTIC foley catheters are soft and supple at body temperature providing maximum patient comfort.

✻ Made from implant tested PVC, SIMPLASTIC foley catheters are less likely to cause urethral irritation.

The new
SIMPLASTIC
routine-use foley catheters
Simply better for your patient

J. G. Franklin & Sons,
P.O. Box 11, High Wycombe, Bucks.,
HP12 3TD, England.
A division of G. D. Searle & Co Ltd.

Further information will be supplied promptly upon request
Simplastic is a registered trade mark

BURNS

Including Thermal Injury

The Journal of the International Society for Burn Injuries

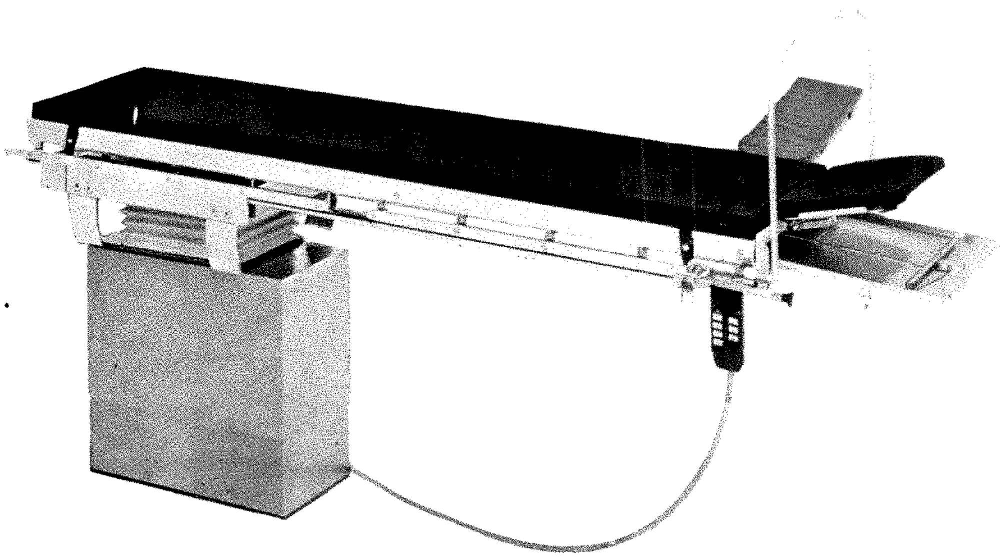
Executive Editor: J. ELLSWORTH LAING, F.R.C.S., Odstock Hospital, Salisbury, Wiltshire

To counter the high mortality and morbidity caused by burn injuries needs the teamwork of a wide range of specialists: treatment of the patient can involve plastic, paediatric and orthopaedic surgeons, biologists, immunologists and bacteriologists, while the rehabilitation of the patient can need the efforts of occupational therapists, physiotherapists, psychiatrists and social workers. This new journal is published to foster the exchange of information amongst all those engaged in preventing and minimizing the effects of burn injuries. *Burns* is sponsored by the International Society for Burn Injuries, whose aims are to transcend national boundaries in improving the prevention and care of burns by education, research, practical advice and assistance, and the encouragement of co-operation between all countries and specialists.

Published quarterly Annual Subscription £8·50

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

Just 4 bolts and a compressed air line



that's all it takes to install the KIFA H3 Table

- ★ The most advanced operating table system available
- ★ Reduces patient handling
- ★ Provides unequalled x-ray facilities ★ Easily cleaned
- ★ Utterly reliable ★ Quick turn-round of patients

Table tops available for general, urological, gynaecological, orthopaedic and micro-surgery. Sierex will be pleased to supply details on request.

Sierex

Sierex Limited
15/18 Clipstone Street, London, W1P 8AE, 01-580 2464
Branches in *Aberdeen, Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester and Reading.*
Agents in *Belfast, Newcastle and Newport.*

The single solution
for parenteral nutrition

Aminoplex 5

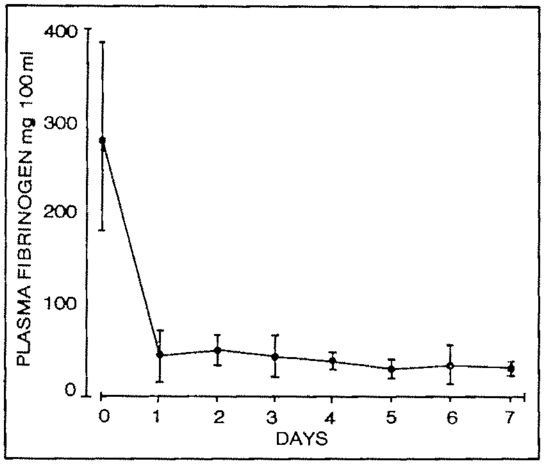
1 litre three times per day provides 15g. of utilisable nitrogen and 3000K calories; the nutrient content being derived from synthetic L-Form amino acids, sorbitol and alcohol.

Geistlich
Chester

In co-operation with Salvia-Werk G.m.b.H., Homburg/Saar, W.Germany.

Medical literature
available from:
Geistlich Sons Ltd.,
Newton Bank,
Long Lane,
Chester CH2 3QZ.
Telephone
Chester 47534-7

A new concept in the control of occlusive vascular disease.



Mean plasma fibrinogen level ± SD in 9 patients with venous thromboses. Arvin 2 units/kg body weight intravenously every 12 hours. From Pitney WR, (1971). Thromb Diath Haemorrh, 45, 43.

Its name is Arvin.

This unique drug is now available to specialists, for routine anticoagulant therapy, and to researchers into thromboembolic disorders.

Arvin reduces plasma fibrinogen to a level that maintains marked hypocoagulability without serious spontaneous bleeding complications. This desirable effect is achieved through the specificity of Arvin for fibrinogen—other clotting factors are unaffected.

The consistent does-effect relationship of Arvin allows simple and precise methods of control.

On this basis, we recommend Arvin wherever controlled therapeutic defibrination is desirable.

Full prescribing information, and clinical evidence from studies on the broad range of thromboembolic disorders, are available on request.

Arvin
ancrod

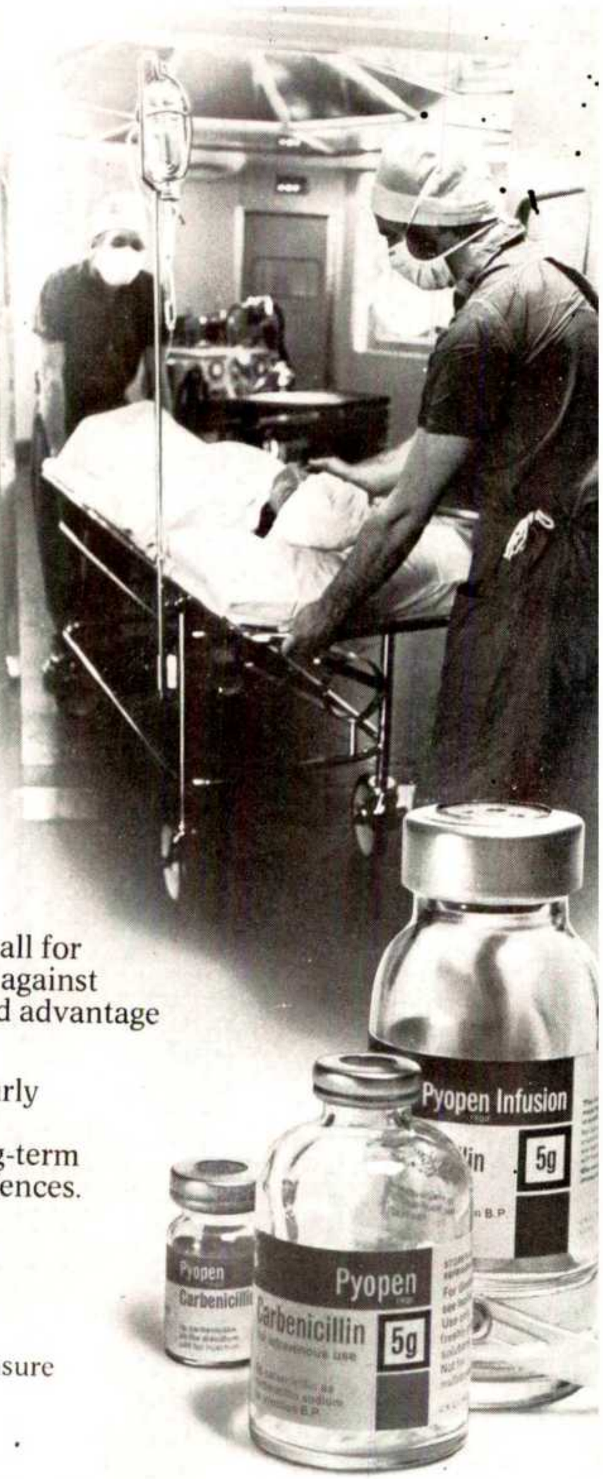
controlled therapeutic defibrination.

Berk Pharmaceuticals Shalford, Surrey.

J4591

Arvin is a registered trademark

When pseudomonas threatens...



Pyopen

The skill of the surgical team, hours in the theatre, the most advanced techniques in the world . . . and infection can still throw the outcome into jeopardy.

Systemic pseudomonas or proteus infections call for Pyopen. Only Pyopen offers you good activity against these Gram-negative organisms with the added advantage of penicillin safety.

Intravenous Pyopen, at a dosage of 5g 4–6 hourly will rapidly control many of these dangerous infections. And Pyopen is also suitable for long-term therapy and for patients with lowered host defences.

Adult Dosage
5g I.V. 4–6 hourly.
In patients with renal impairment dosage may be reduced; monitoring is advisable in these cases to ensure adequate serum antibiotic levels.
Contra-indication
Penicillin hypersensitivity.
Side-effects
As with other injectable penicillins. In rare cases, skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Pyopen – by infusion or injection

Further information is available on request.
Pyopen* (carbenicillin sodium B.P.) is a British product originated by
Beecham Research Laboratories, Brentford, England. *regd.

The British Journal of Surgery

Vol. 62 : No. 6 : June 1975

Br. J. Surg. Vol. 62 (1975) 421–430

Hepatic resection*

G. B. ONG AND N. W. LEE†

SUMMARY

One hundred and twenty-five hepatic resections were done in the University Surgical Unit at the Queen Mary Hospital, Hong Kong, from 1964 to 1974 for conditions varying from primary hepatoma and recurrent pyogenic cholangitis to spontaneous rupture of the liver due to a bleeding haemangioma.

The overall mortality was 17·6 per cent. A case was classed as an operative death unless the patient was discharged from hospital. There has been long term survival after resection for primary carcinoma of the liver and no mortality when resection was carried out for benign conditions.

IN 1953 we performed a subtotal gastrectomy for a carcinoma of the stomach with resection of the lateral segment of the left lobe of the liver. The patient made an uneventful recovery but subsequently died of metastases 3 years after the initial operation. However, it was not until 1955 that we carried out hepatectomy for primary hepatoma with any frequency at the Kowloon Hospital, Hong Kong. All the records accumulated during the period from 1955 to 1963 were lost, except for those of 1 patient who has been followed up since.

Patients

Over a period of 10 years, from 1964 to 1974, 125 resections of the liver were carried out; one of these, as mentioned, was done at the Kowloon Hospital, the remainder being performed at the Queen Mary Hospital, Hong Kong. There were 83 males and 42 females, giving a sex ratio of 2 : 1.

Table 1: CONDITIONS FOR WHICH LIVER RESECTION WAS CARRIED OUT, 1964–74

	Sex			Age (yr)	
Pathology	M	F	Ratio	Range	Average
Hepatocellular carcinoma	59	11	5 : 1	9½ mth–85 yr	50
Recurrent pyogenic cholangitis	15	23	1 : 2	20–77	49
Trauma	3	1	3 : 1	17–52	35
Cyst	0	2	0 : 2	63–76	70
Liver abscess	3	1	3 : 1	45–59	51
Carcinoma of colon	1	2	1 : 2	58–75	64
Carcinoma of intrahepatic duct	2	0	2 : 0	47–58	53
Leiomyosarcoma of jejunum	0	1	0 : 1	—	44
Ruptured haemangioma	0	1	0 : 1	—	43

Lesions of the liver requiring resection

Table 1 shows the conditions for which liver resection was carried out.

Primary carcinoma of the liver

There was a total of 70 cases of carcinoma of the liver where resection was possible; of these, 9 were cholangiohepatoma and 61 hepatocellular carcinoma. Of the 61 cases of hepatocellular carcinoma, cirrhosis was present in 35, while among the cases of cholangiohepatoma it was found in 3.

The incidence of hepatocellular carcinoma with cirrhosis of the liver has been reported as 73·1 per cent (Tull, 1932) and 89 per cent (Stewart, 1931). Hou (1958) found that of the 66 per cent of his series with primary liver cancer associated with cirrhosis, 46·5 per cent also had clonorchiasis. Wang and Li (1963) studied 130 resected cases of primary carcinoma of the liver and reported an association of primary cancer with cirrhosis in all except 2 cases. This is of importance as the cirrhotic liver does not take kindly to resection, for even when the liver is mildly cirrhotic but the resection extensive the patient often succumbs to liver failure. Lin (1966) stated that when the liver is cirrhotic, right or left hepatectomy is contraindicated. While it is true that massive resection in a cirrhotic liver often ends in liver failure, at times the resected liver is found to have very little functioning tissue. Hence, a hepatectomy in such cases is still compatible with survival.

Eighteen out of the 70 cases were admitted because the hepatoma had ruptured. The mechanism of rupture has been previously discussed (Ong et al., 1965; Ong and Taw, 1972).

As a result of cirrhosis a number of patients developed portal hypertension, and the resulting bleeding could have been the cause of death in the postoperative period.

---

* Based on a lecture delivered at the Repatriation Hospital, Concord, New South Wales, Australia.

† Department of Surgery, University of Hong Kong, Hong Kong.

Recurrent pyogenic cholangitis

Some cases with recurrent pyogenic cholangitis require resection of the liver. In the present series it was done for intrahepatic stones which most frequently formed in the lateral segment of the left lobe. The bile ducts were thickened, dilated and contained infected bile with stones (*Fig.* 1). The liver parenchyma showed degeneration and was often shrunken to such an extent that it was almost a fibrotic bag. There was usually a stricture at the junction between the medial and the lateral segments of the left lobe and this was possibly the cause of stone formation in the liver. As the bile was invariably infected, resection of the liver often resulted in subphrenic abscess or biliary fistula and occasionally septicaemia. Altogether 38 such cases were subjected to resection of the liver.

Trauma to the liver

Although the incidence of trauma to the liver is increasing owing to more road traffic accidents, the number of cases that require resection is relatively small. In the 10 years of this study there were only 4 cases in which it was necessary to remove a lobe of the liver. In 2 of them the right lobe of the liver had a stellate fracture which compromised the blood supply so that it was necessary to remove this lobe. In 1 patient the right lobe had a linear fracture which was repaired, while the lateral segment of the left lobe was removed. In the remaining patient the fracture was over the medial segment of the left lobe and it was necessary to perform a resection because of necrosis. These patients were relatively young when compared with the patients with other conditions necessitating hepatectomy.

Cysts

There were 2 patients with a cyst in the left lobe of the liver; both patients were elderly females. The cysts were simple and did not contain any malignant tumour.

Liver abscess

During the last 5 years of the study 4 cases of liver abscess were seen. In 1 case an extended right hepatectomy was carried out because the abscess was mistaken for a carcinoma of the liver. On examination, the resected liver contained hardly any normal liver tissue (*Fig.* 2). In another case a right hemihepatectomy was carried out because of haemorrhage into the abscess. Both of these cases were subsequently proved to be amoebic liver abscesses. In addition to these cases there were 2 cases of liver abscess which had initially been drained and subsequently developed a discharging sinus. No amoebae were demonstrated either in the pus or in the wall of the abscess in these cases. Culture was originally sterile, but after drainage pyogenic bacteria were isolated. These were probably the cause of the discharging sinus (*Fig.* 3).

Carcinoma of the colon with metastases to the liver

There were 3 cases in this group; 2 females and 1 male. The male and 1 female patients had a carcinoma of the hepatic flexure which had invaded the right lobe of the liver; the rest of the liver was normal (*Fig. 4*). The third patient had a carcinoma of the sigmoid colon with metastases to the medial segment of the left lobe. The liver was also cirrhotic.

Carcinoma of the bile ducts

There were 2 cases of carcinoma of the right hepatic duct. The patients were markedly jaundiced; the liver was not cirrhotic but was deeply stained. Both were males, one aged 47 and the other 58. Histologically, the tumours were shown to be adenocarcinoma arising from the right hepatic duct.

Leiomyosarcoma of the jejunum

In 1 case a leiomyosarcoma of the jejunum was found with secondaries in the right lobe of the liver. The rest of the liver was normal.

Bleeding haemangioma

A case of bleeding haemangioma was seen in this series. A huge cavernous haemangioma arising from the right lobe of the liver and extending to the medial segment of the left lobe occurred in a female patient. The rest of the liver was normal. The left lobe was rather hypertrophic and the cut section of the resected specimen showed there were some fibro-fatty tissues at the centre (*Fig.* 5).

Clinical features

Abdominal mass

This was by far the most common finding in the patients undergoing liver resection. It was present in all the patients with primary carcinoma of the liver, and in addition the 4 cases of liver abscess also had a mass palpable in the upper part of the abdomen. The patients with a cyst presented with a mass in the upper abdomen which moved with respiration and was non-tender. In carcinoma of the bile duct the palpable mass in the upper quadrant could be identified as a uniformly enlarged liver. The patient with secondary leiomyosarcoma also had an enlarged liver with irregular masses studded over it.

Abdominal pain

Abdominal pain was a constant finding and was usually confined to the right upper quadrant, occasionally radiating to the back or referred to the shoulders. This was present in the majority of the patients with carcinoma of the liver and in the patient with a ruptured haemangioma. The pain was rather sudden and was described as 'bursting' in nature in all cases of ruptured hepatic tumour. Sometimes it was associated with the rapid onset of shock.

Intraperitoneal haemorrhage

This occurred in 18 cases of ruptured carcinoma of the liver. Traumatic rupture of the liver produced intraperitoneal haemorrhage with very severe pain and the patient rapidly went into shock. The amount of fluid varied. In primary hepatoma ascites might be present; and any bleeding, even if severe, would yield only heavily bloodstained fluid on paracentesis.

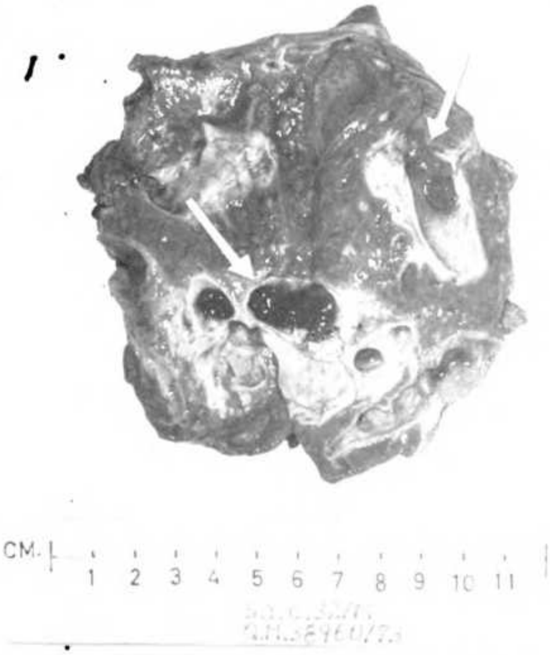


Fig. 1. Resected specimen of the lateral segment of the left lobe of a liver. The ducts are dilated, fibrotic and contain stones.

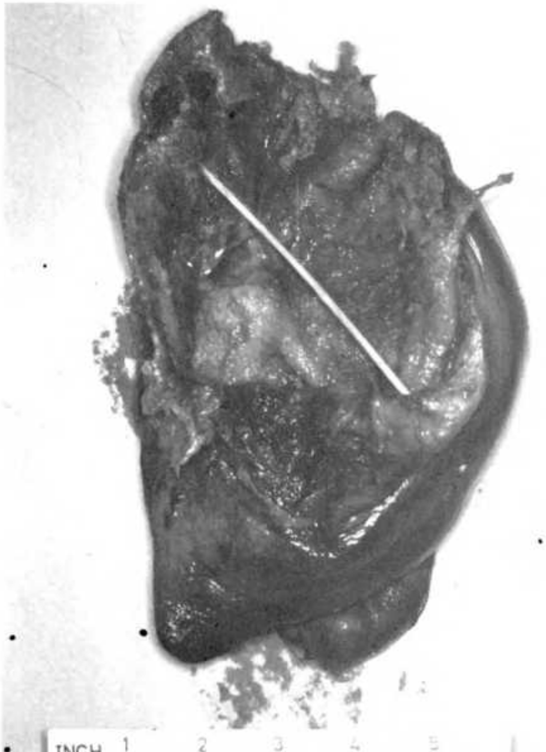


Fig. 2. Specimen of destroyed liver due to amoebiasis. There is hardly any normal liver tissue.

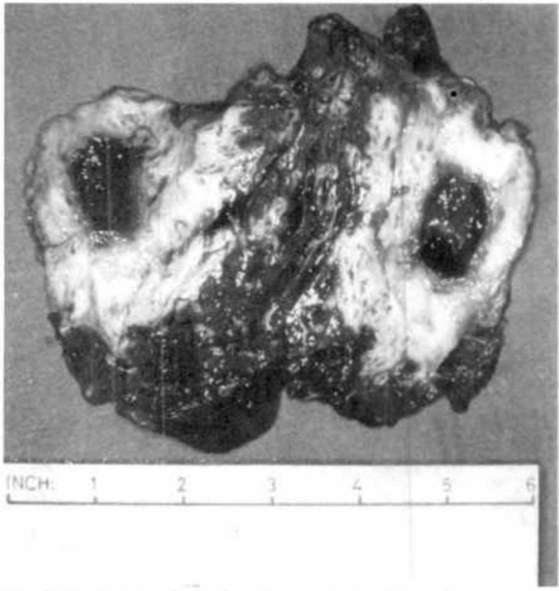


Fig. 3. Persistent sinus after drainage of a liver abscess which was treated and cured by resection.

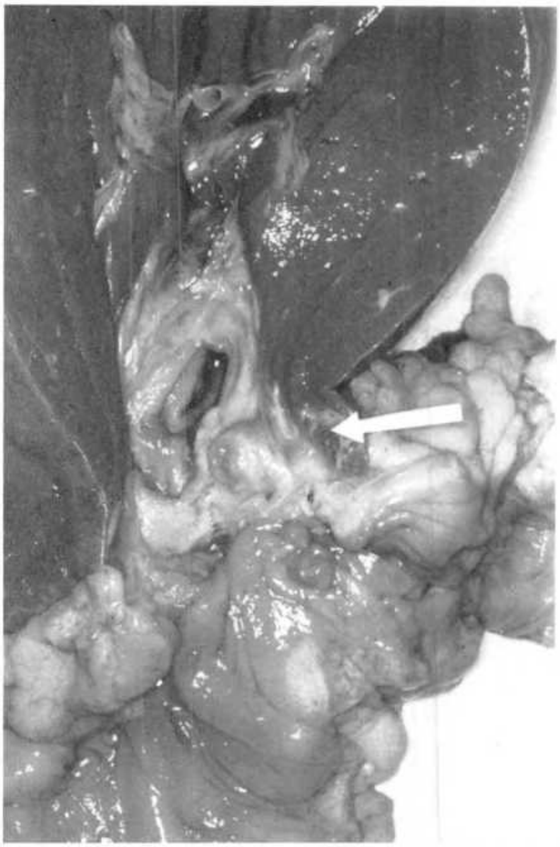


Fig. 4. Carcinoma of the hepatic flexure invading the right lobe of a liver. This was treated by right hepatectomy and right hemicolectomy.

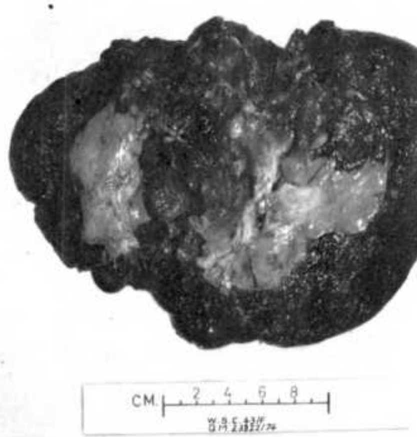


Fig. 5. Bleeding haemangioma of the liver.

Weight loss

Weight loss was found in 37 of the 70 cases of primary hepatoma. It was not found in recurrent pyogenic cholangitis, traumatic rupture, cysts or in the case of a ruptured haemangioma. A variable degree of weight loss was noticed in carcinoma of the colon with liver secondaries, while the patient with carcinoma of the bile duct had marked loss of weight. The patient with leiomyosarcoma of the jejunum had also lost weight.

Anorexia

Approximately half the patients with primary hepatoma complained of anorexia. It was also present in the patients with recurrent pyogenic cholangitis, liver abscess and other malignancy, but was absent in these with traumatic rupture of the liver, cyst and ruptured haemangioma.

Preoperative investigations

Except for emergency operations for bleeding, all the cases were subjected to laboratory investigations.

Laboratory findings

Anaemia was present, although of a mild degree, in all the cases of primary hepatoma. Polycythaemia in primary hepatoma, as reported by McFadzean et al. (1958), was not present in any of these patients. Leucocytosis was also an occasional finding in primary hepatoma and was noticeably absent in the 4 cases of liver abscess, while the white cell count was moderately raised in all the cases of recurrent pyogenic cholangitis. α-Fetal protein gave positive results in 70 per cent of the cases of hepatocellular carcinoma. This test was invariably negative in the patients with cholangiohepatoma.

The liver function tests were of little value except in a case of carcinoma of an intrahepatic duct when the bilirubin was markedly raised. The alkaline phosphatase was not helpful except in the case with obstructive jaundice.

X-ray examination

When X-ray examination showed a soft tissue shadow at the upper abdomen a barium meal study occasionally demonstrated displacement of the stomach, indicating a hepatic mass.

Splenovenography

The usefulness of this investigation lies in the fact that the portal vein may be obliterated as a result of tumour invasion. Should the obstruction extend beyond the bifurcation of the portal vein, then surgical treatment is contraindicated. Portal hypertension is also demonstrated by this procedure.

Hepatic arteriography

Hepatic arteriography is useful in differentiating a malignant lesion with new vessels from a benign one, when the vessels are only displaced.

Scanning of the liver

Scanning with ^{99}Tc does not differentiate a malignant tumour from a benign one. When the lesion is small, scanning usually does not demonstrate any filling defect, and then it is necessary to depend on other investigations for diagnosis as a therapeutic guide.

Peritoneoscopy

Peritoneoscopy is a useful means of diagnosing a liver condition requiring a resection. A primary hepatoma as well as secondary tumour can be seen on the surface. Biopsy under direct vision can then be done and a histological diagnosis made of the lesion. In addition, it is useful in demonstrating the cirrhotic state of the liver. However, peritoneoscopy has many blind spots. The posterior surface of the liver is obscured by adhesions. Any centrally situated lesion will be out of the field of vision.

Inferior vena cavogram

An inferior vena cavogram may occasionally be useful, especially in carcinoma when the tumour has invaded the inferior vena cava, in which case resection is contraindicated.

Preoperative preparations

In most of the cases undergoing elective operation the nutrition should be maintained, and intravenous hyperalimentation will help in getting the patient fit for a major operation. A diet rich in vitamins should be given. Supplementary vitamin A in liquid solution with 10 000 units of vitamin B should be given daily, to which 500 mg of vitamin C may be added. When the prothrombin time is prolonged vitamin K 50/100 mg may be given by intramuscular injection. A diet rich in protein with a high carbohydrate and moderate fat content should be given. Anaemia should be corrected by blood transfusion.

Contraindications to operation

Operative treatment is contraindicated under the following circumstances:

1. *Metastatic spread*: When metastases are demonstrated in the lungs or the bones, surgical exploration should not be carried out. When there are secondaries in the supraclavicular lymph nodes, particularly in

cholangiohepatoma or carcinoma of the colon, operative treatment is out of the question.

2. *Jaundice*: The presence of jaundice is not a contraindication to operation, but may be a contraindication to resection of the liver. Occasionally an hepatocellular carcinoma will spread into the common hepatic duct and produce obstructive jaundice. In such cases resection is not compatible with a cure.

S. A. T., a male patient aged 53 years, was admitted in 1969 because of obstructive jaundice. An operation was performed on 14 July 1969 when a right extended hepatectomy was carried out. He survived 5 months before dying of multiple secondaries in the remnant of the liver (*Fig. 6*).

3. *Ascites*: The presence of ascites is a contraindication to operation, as it indicates that the liver is failing and will not tolerate any operative procedure.

4. *Biochemical changes*: Biochemical changes showing poor liver function indicate that the patients, particularly those with primary hepatoma, with cephalin flocculation of over 3 units, bromsulphthalein retention of over 35 per cent and serum albumin below 2·5 g per cent or prothrombin time below 60 per cent, are unlikely to survive an operation and hence surgery should not be done.

Operations currently practised

Left medial segmental resection

This is an operation that is seldom carried out. It was done only twice in this series; once for trauma to the liver in which the medial segment was completely necrotic and bleeding. It was also done for a ruptured carcinomatous nodule situated in the medial segment of the left lobe. This man subsequently died of bleeding varices. The artery, portal veins and segmental duct were dissected out; these were found half an inch deep to the insertion of the ligamentum teres. The segment was then resected from in front backwards until the medial segmental hepatic vein was exposed and ligated. The segment was removed and the edges of the liver remnant were brought together.

Left lateral segmental resection

In performing left lateral segmental resection the left coronary ligament was freed from the undersurface of the diaphragm. The free end of the coronary ligament contained a few small vessels and in a cirrhotic liver bled profusely. The raw area left on the diaphragm had to be sutured with atraumatic catgut.

After the left lateral segment had been freed, the forceps holding its tip were depressed to expose the lateral segmental hepatic vein. A little dissection freed it from the inferior vena cava. Often the medial segmental vein joined it before they became a single vein draining into the inferior vena cava.

In order to ligate the lateral segmental vein it was occasionally necessary to dissect into the substance of the liver. After its ligature and division, the liver containing the tumour or stone was rotated forwards so that the lateral segment of the left lobe was brought out of the abdomen. The segmental hepatic artery, the segmental duct and the segmental branch of the portal vein were ligated as they ran near the posterior border of the left lobe of the liver. After ligating the artery, vein and the duct, the lateral segment of the liver was ready for division. Further haemostasis of the transhepatic segmental hepatic veins could be attained by suture ligatures.

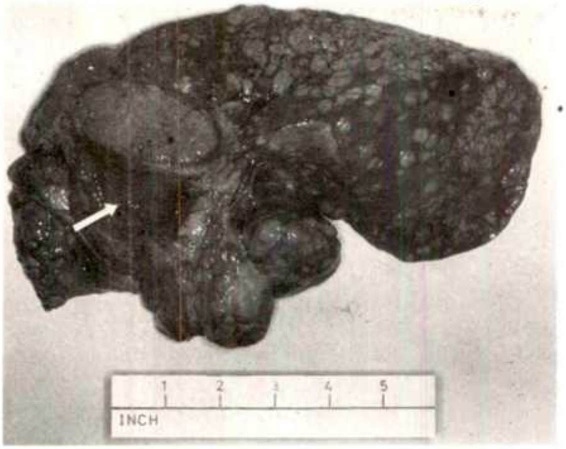


Fig. 6. Secondaries which appeared in the remnant of a hypertrophic liver. Arrow points at the hepaticojejunostomy.

Left hemihepatectomy

In this operation the liver was divided along the principal plane dividing the right and left lobes of the liver. A Mayo-Robson incision was made and the left coronary ligament was divided and detached. The left hepatic vein was dissected out, divided between clamps and stitched as for lateral segmental resection. After division of the left branch of the portal vein, hepatic artery and hepatic duct, the left lobe of the liver became a dusky colour or sometimes even black. The division of this lobe of the liver was now made by cutting through the capsule of the liver and, with the handle of the scalpel, the intersegmental veins were teased out and ligated or stitched. The cut edge of the liver was either sutured with a series of interrupted or continuous catgut sutures, or, in most cases, after controlling the bleeding from the raw surface a piece of Surgicel was placed over it and then pieces of Gelfoam to cover the whole raw area. The Gelfoam was stitched to the capsule of the liver. This method resulted in good healing.

Right hemihepatectomy

Exploration of the back of the liver was first carried out. This avoids division of the structures at the porta hepatis which makes it necessary to resect the devascularized liver. If the tumour has infiltrated the inferior vena cava, resection will result in either part of the tumour being left behind or the inferior vena cava being torn beyond repair.

After exploration, attention was focused on the structures at the porta hepatis. Division and ligation of these structures were performed. Next, the hepatic vein was dealt with.

If the coronary ligament had been freed when the hepatic veins were explored, the liver could be

TABLE II: COMPLICATIONS IN 125 LIVER RESECTIONS

Complication	No. of cases	%
Haemorrhage	4	3
Biliary fistula	11	9
Infection		
Septicaemia	6	5
Subphrenic abscess	13	10·4
Liver abscess	1	0·8
Pleural effusion	4	3

delivered out into the wound. In so doing, there would be a kink of the inferior vena cava. Lin (1966) believed that the kinking of the inferior vena cava would impede the venous return and could cause cardiac arrest. Hence he devised his finger-fracture technique so that the hepatic veins could be divided within the liver substance. Division and removal of the liver were then carried out in the same manner as for left hemihepatectomy. However, kinking of the inferior vena cava can be lessened if the lower hepatic veins are dissected out first and ligatured. This can be done with the liver in the abdomen, and leaves the uppermost hepatic vein which is short and can be found at the bare area of the liver.

In dividing the uppermost hepatic vein over the kink of the inferior vena cava a piece of the inferior vena caval wall might inadvertently be included. If this occurred a transfixion of the vein would inevitably cause the suture ligature to slip and severe bleeding might take place. It is therefore wise, at this stage, to have ready a vascular clamp of the Satinsky type. Should such an accident happen the inferior vena cava could be clamped and sutured.

Extended right hepatectomy

Occasionally, a tumour is large enough to require removal of the liver to the right of the falciform ligament. The exploration and method of dealing with the hepatic veins were similar to those for right hemihepatectomy. The ligature of structures at the porta hepatis was similarly carried out. However, the left medial segmental artery and the right segmental portal vein with the segmental duct have to be dealt with in this procedure. The lateral segmental duct, artery and portal vein were preserved and found to be half an inch deep to the ligamentum teres. At this stage of the division of the medial segmental duct it would be prudent to place a T-tube into the left hepatic duct, for it would prevent damage to the lateral segmental duct.

The raw surface of the liver was again dealt with either by suturing the capsule together or by placing some haemostatic agents and stitching them to the capsule of the liver. If the falciform ligament is not involved it provides a convenient piece of material to stitch over the raw surface.

Extended right hepatectomy represented a removal of between 75 and 80 per cent of the liver tissue, while a right hemihepatectomy removed between 55 and 60 per cent, and removing the left half of the liver represented 45–50 per cent of liver tissue by weight.

Postoperative care

Patients undergoing liver resection required intensive supportive treatment until the remaining liver had regenerated sufficiently to take care of the metabolic needs of the body. Broad spectrum antibiotics were given to prevent chest infection.

Care of the drain

Whenever the chest was opened an underwater seal drain was inserted and removed on the third or fourth postoperative day. An X-ray of the chest was taken on the day after the operation and repeated after the drain had been removed.

Subsequent pleural effusion would require thoracocentesis. A subdiaphragmatic drain was usually placed in the space formerly occupied by the resected liver. A small amount of serosanguineous fluid was always present, but occasionally there was an excessive amount of ascitic fluid in which case the drain was removed. This would prevent excessive loss of ascitic fluid. The drain occasionally might be blocked by a blood clot and therefore too much reliance must not be placed on its efficiency to demonstrate the presence of bleeding. A large distended abdomen with the patient going into shock would indicate postoperative bleeding and steps should be taken to control it.

Administration of fluids

After blood replacement and administration of fluid, 25 per cent glucose should be given through the inferior vena cava via a cut-down; 200 g of glucose were given daily and adequate vitamins were also administered. Oral feeding can usually be restarted on the second or third postoperative day. A high protein diet should be avoided as it has been shown by Pack and Molander (1960) that too high a protein intake might cause intoxication in a patient with massive resection of the liver.

Complications

These are detailed in *Table II.*

Postoperative haemorrhage

Haemorrhage occurred postoperatively in 4 patients undergoing hepatic resection, all for carcinoma of the liver, and in 1 instance the bleeding was into the pericardium from the upper part of the inferior vena cava. The patient was explored again and subsequently made an uneventful recovery. The other 3 cases had bleeding from the collaterals resulting from portal hypertension in a cirrhotic liver. At the conclusion of the first operation there was no bleeding as every part of the raw surface had been run over with atraumatic catgut. Subsequently, further collaterals which had been missed started bleeding and they were controlled by suturing.

Biliary fistula

Eleven cases (9 per cent) had a biliary fistula. Four patients had undergone resection for carcinoma of the liver and in 1 instance it had been a left hepatectomy in which the duct had been closed with interrupted silk in good approximation. However, a fistula developed. A biopsy taken at the margin showed that carcinomatous cells were still present. In one of these cases after an extended right hepatectomy a T-tube was inserted and the medial segmental duct was carefully closed with interrupted fine silk. Nevertheless, leakage occurred but the fistula healed spontaneously.

Six cases had had resection for recurrent pyogenic cholangitis. In each instance the closure had been performed with interrupted silk. Subsequently, the incidence of biliary fistula was lowered by reverting back to closure with atraumatic catgut and then suturing the liver capsule over it. In 1 case the biliary fistula developed after a right hepatectomy for traumatic rupture of the liver. The fistula healed spontaneously without any further operation.

Infection

Infection accounted for the greatest number of complications in the patients undergoing hepatic resections. There were 6 patients who developed septicaemia, and Gram-negative enteric organisms were cultured from the blood. In 3 of them the hepatectomy was for hepatocellular carcinoma while in the other cases for recurrent pyogenic cholangitis.

Subphrenic abscess occurred in 13 patients (10·4 per cent). The abscesses usually developed following incomplete or inefficient drainage of the space left after resection of the liver. Suction drains were used but even this could not completely prevent the development of subphrenic abscess.

Pleural effusion

Pleural effusion occurred in 4 cases and was confined to cases of right hepatectomy in which the chest had been opened. In 2 of them the effusion kept recurring and malignant cells were found in the pleural fluid. In 1 case a combination of right hepatectomy and pulmonary lobectomy caused pleural effusion of the left pleural cavity. Rupture of the spleen occurred during thoracocentesis.

Operative mortality

After undergoing hepatectomy every patient who did not leave the hospital was considered an operative mortality. Thus, a case might have undergone an operation and then died of liver failure 45 or 60 days after operation. This would still be considered as an operative mortality.

There were 22 deaths out of 125 resections, giving an overall mortality of 17·6 per cent. Of these, 15 had had resection for primary hepatoma; 7 of these 15 died in the first 5 years of the series, that is, from 1964 to 1969, when 22 resections were performed, giving a mortality of 32 per cent. In the succeeding 5 years, from 1969 to 1974, there were 48 resections with 8 deaths, giving a mortality rate of 17 per cent. There is therefore a definite drop in operative mortality. This results not only from improved technique but also from better selection of the best operation for a particular case. The following case report is an example of such selection.

Y. S. K., a female patient, was admitted in 1972 because of an enlarging mass which was found to be a hepatoma involving the right lobe of the liver. An hepatic arteriogram showed that the tumour arose from the upper division of the right lobe (*Fig.* 7). This was confirmed by a splenovenogram (*Fig.* 8). Peritoneoscopy not only revealed the presence of the tumour but also cirrhosis of the liver. A needle biopsy confirmed the diagnosis of hepatocellular carcinoma.

At operation it was decided that the tumour should be removed, sparing the inferior division of the right lobe. Accordingly, the segmental duct, the branch of the hepatic artery and the branch of the portal vein to this division were preserved. The rest of the right lobe was then removed. Examination of the operated specimen showed that the tumour had a narrow rim of normal tissue (*Fig.* 9).

The patient had a postoperative haemorrhage at the site where the superior branch of the hepatic vein drained into the inferior vena cava. This had previously been stitched, but a new tear in the upper part of the inferior vena cava extending into the atrium was found at the second operation. This was sutured and the patient made an uneventful recovery. Subsequently, a hepatic arteriogram showed that this segment was functioning and scanning showed a good-sized segment. This patient has been followed up for the past 2 years and she is quite well without any evidence of recurrence of her disease or metastases (*Fig.* 10).

It is possible that this patient would have died had the whole of her right lobe had been removed. The amount of liver tissue that was functioning and removed at operation was minimal.

Among the 70 resections for primary hepatoma 34 patients had cirrhosis of liver and there were 9 deaths, giving a mortality rate of 26 per cent. The causes of death were liver failure in 5 cases, septicaemia in 2 and hypovolaemic shock following uncontrolled haemorrhage in 2. The remaining portion of a very cirrhotic liver did not appear to be able to regenerate sufficiently to take over the function of the removed segment or lobe. Furthermore, bleeding in cirrhotics, especially from collaterals, was always profuse. Even at the very early stage of resection when the liver was being mobilized, much blood could be lost from these collaterals. The haemorrhage could be controlled by packing and subsequently with running stitches. In an attempt to replace blood loss with massive transfusion, a coagulation defect could develop and this was often the cause of death.

Septicaemia was also much more likely to occur in these patients, for they tolerated infection poorly. Two of the cases dying of septicaemia belonged to the group of patients with recurrent pyogenic cholangitis that required liver resection.

Traumatic rupture of the liver occurred in 2 patients with multiple injuries; both patients died of cardiac arrest following irreversible shock shortly after operation. Although the resections were extensive, the other benign conditions in this series did not give rise to any mortality. None of the patients operated on for carcinoma of the colon with liver metastases died within the postoperative period.

The patient with leiomyosarcoma who died of cardiac failure was known to have cardiac ischaemia.

Two cases of carcinoma of the bile ducts were operated on; one was an extended right hepatectomy and the other a right hepatectomy. Reconstruction of the biliary tract was in each instance by hepatico-jejunostomy. One patient developed a subphrenic

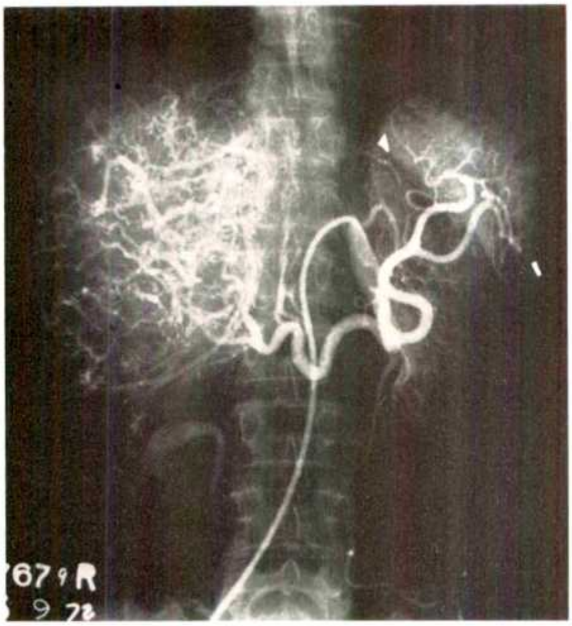


Fig. 7. Hepatic arteriogram in a primary carcinoma of the liver. Note the new vessels entering the tumour. The right inferior division is normal.

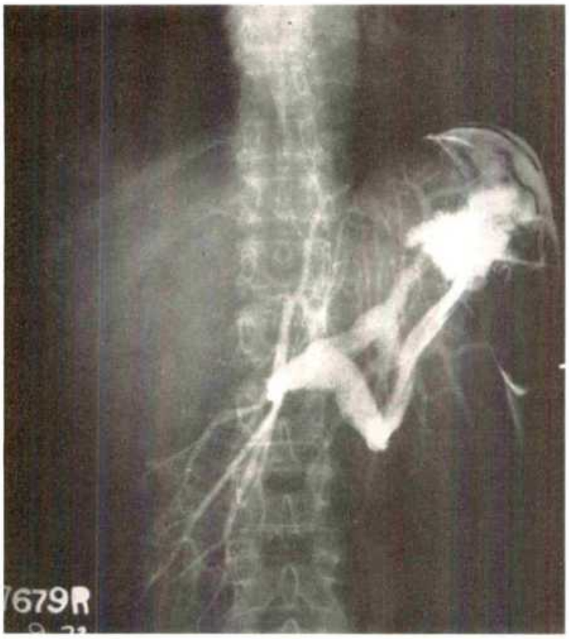


Fig. 8. Splenovenogram showing infiltration of cancer in the segmental vein.

abscess but both died of liver failure. Their jaundice never subsided and their condition deteriorated until they went into coma and died 40 and 48 days after operation respectively.

The survivors

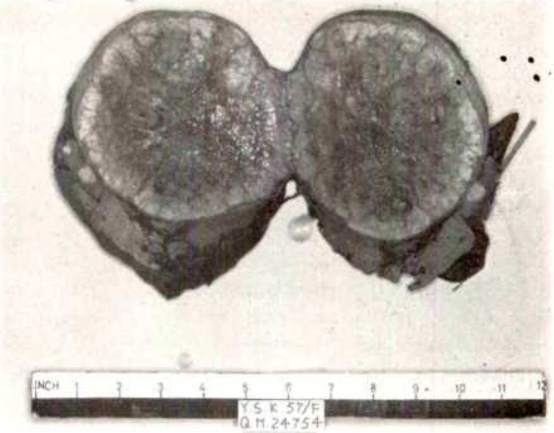


Fig. 9. Resected specimen of a liver showing a large carcinoma.

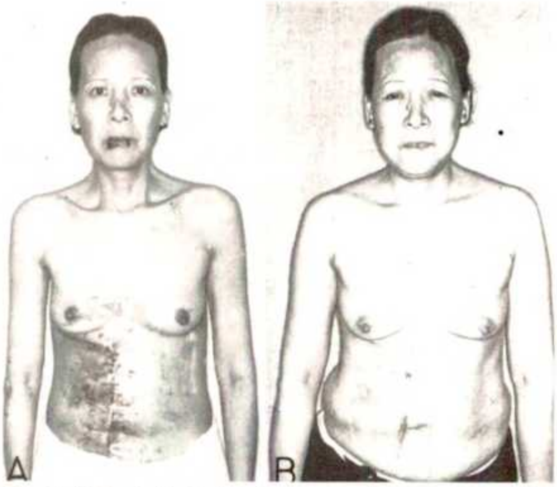


Fig. 10. Patient who had had a primary hepatoma resected; (*A*) during convalescence, and (*B*) 2 years afterwards.

Of the 103 patients who survived hepatic resection, 39 subsequently died from 5 to 41 months after operation, the average being 10 months. All died of their original disease. One patient with recurrent pyogenic cholangitis died 18 months after hepatectomy. She developed leakage of bile through the old drainage wound which was persistent and it was necessary to explore the bile ducts to close this biliary fistula. She died of uncontrolled haemorrhage due to a coagulation defect.

Carcinoma of the colon with metastases to the liver accounted for 2 deaths. One was a female patient who survived a right hepatectomy with the right hemicolectomy carried out in continuity. This patient was operated on in 1968. She survived for 18 months but eventually died of her disease.

Up to the present time 64 cases are still alive out of the original 125. *Table III* shows that 19 of the patients with carcinoma of the liver are alive and the longest survival is now 13 years. This is a patient who had a left hemihepatectomy done in 1962 for a ruptured hepatoma and who emigrated in 1971. The second longest survivor is a man with hepatoma which ruptured while being investigated. An emergency extended right hepatectomy together with partial excision of the diaphragm was carried out. This patient is still alive and well. A female who was operated on for a hepatoma of the left lobe with two secondary nodules on the medial segment is alive and well today, 5 years after the operation. Of the remaining surviving patients, 1 was operated on in 1971, 3 in 1972, 4 in 1973 and 8 in 1974.

Of the patients with other conditions who are still alive after hepatic resection (*Table IV*), one had a carcinoma of the sigmoid colon with metastases to the liver for which a total colectomy and left medial segmental resection was carried out 15 months ago.

Thirty-five of the cases with recurrent pyogenic cholangitis are still alive 6 months to 10 years after operation.

Of the patients with traumatic rupture, one who had a right hemihepatectomy done 7 years ago and another who had a left medial segmental resection performed 3 years ago are alive at the present time.

The 2 patients with a cyst which was treated by left hemihepatectomy have survived without problems for 2 years and 5 years respectively.

Of the patients with liver abscess who were operated on, one had an extended right hepatectomy which was carried out 4 years ago. This was a patient who was operated on because of a mistaken diagnosis of hepatoma arising from the right lobe of the liver. As the lesion was soft it was thought to be a necrotic tumour. No aspiration of the abscess was carried out. He made an uneventful recovery and was discharged from hospital after 2 weeks. He has been followed up since and the liver has regenerated to its original size and he is at the present moment quite well (*Fig.* 11).

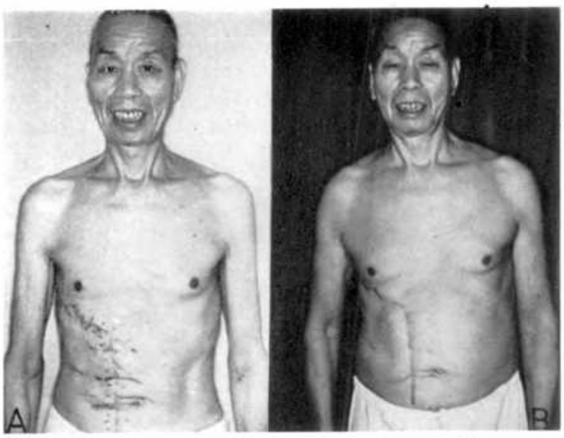


Fig. 11. Patient who had undergone resection of a liver abscess; (*A*) 6 months, and (*B*) 4 years following operation.

The ruptured haemangioma was operated upon on 6 July 1974; the patient was discharged 10 days after the operation.

Discussion

Certain conclusions can be drawn from the present series.

Operative mortality

Primary hepatoma carried the highest operative mortality, which is understandable because hepatoma is a complication of a cirrhotic liver. Islami et al. (1958) have shown that in rats with carbon-tetrachloride-induced cirrhosis the liver remnant after resection could regenerate and function normally. However, in humans when a cirrhotic liver is resected it does not

Table III: DETAILS OF 19 SURVIVING PATIENTS WHO UNDERWENT RESECTION FOR PRIMARY HEPATOMA

Year of operation	Type of resection	Lesion	No. of cases
1962	Left hemihepatectomy	Ruptured hepatoma	1
1966	Extended right hepatectomy	Ruptured hepatoma	1
1969	Left hemihepatectomy	Hepatoma	1
1971	Left hemihepatectomy	Hepatoma with cirrhosis	1
1972	Right or left hemihepatectomy	Hepatoma with mild cirrhosis	3
1973	Right or left hemihepatectomy or extended right hepatectomy	Hepatoma, 2 with and 2 without cirrhosis	4
1974	Right or left hemipatectomy or extended right hepatectomy	Hepatoma with or without cirrhosis	8

Table IV: DETAILS OF SURVIVING PATIENTS WHO UNDERWENT RESECTION FOR CONDITIONS OTHER THAN PRIMARY HEPATOMA

Lesion	Type of resection	No. of cases	Length of survival to date
Carcinoma of sigmoid colon with metastasis to liver	Total colectomy with left medial segmental resection	1	15 mth
Recurrent pyogenic cholangitis	Left lateral segmental resection	35	6 mth–10 yr
Traumatic rupture	Right hemihepatectomy, left medial resection	2	7 and 3 yr
Liver cyst	Left hemihepatectomy	2	2 and 5 yr
Liver abscess	Extended right hepatectomy	1	4–9 yr
	Left hemihepatectomy	2	
	Right hemihepatectomy	1	
Ruptured haemangioma	Right hemihepatectomy	1	10 d

regenerate into a normal functional unit. There may be islands of regeneration. In fact, the hepatoma most probably arises from one of these regenerated nodules.

As hepatocellular carcinomas are always at an advanced stage when first seen, massive resection is often required. If cirrhosis of the liver is severe, massive resection will always end in death from liver failure. However, with proper selection of cases and correct application of operative treatment the mortality rate should be reduced to an acceptable level.

From 1964 to 1969 the operative mortality from hepatic resection for primary hepatoma was 32 per cent. In 1974 there were 9 resections for primary carcinoma of the liver with only 1 death, a mortality of 11 per cent. Lin (1973) reported a mortality rate of 11·9 per cent in a series of resections for primary hepatoma of the liver. Further, he gave a figure of 19·1 per cent for 5-year survival.

Hepatic resection for secondary carcinoma should carry a very low mortality. In 3 resections for metastasis from carcinoma of the colon there was not a single death. When resection is carried out for a benign non-infective condition there should be no mortality, as shown by results for the cysts and the bleeding haemangioma in the present series. However, when the operation is performed for infected bile ducts with intrahepatic stones, then the mortality is 5 per cent.

Technical difficulties

Exposure of the liver has always been found to be difficult. A correct incision gives a good view of the liver which is fixed to the posterior abdominal wall. The incision that we have employed is a right transrectus incision. On exploration if it is found that the right hepatic resection is necessary the upper end of the incision is extended to the right side of the chest, cutting through the costal cartilage without opening the pleura. However, there is no bar to opening the pleura if a better exposure is required. Smith (1968) preferred a right thoraco-abdominal incision as he considered it desirable to open the chest to minimize the likelihood of air being sucked into the hepatic vein during resection and believed that positive pressure could prevent this action. We have not encountered this problem of air embolism.

Control of haemorrhage

Lin (1966) believed that it was extremely difficult to control haemorrhage from the hepatic veins if they were divided first. We have not found any problem in dividing the hepatic veins. The left hepatic duct is found and ligated fairly easily. There are two veins draining each segment of the liver; the right hepatic veins are much more difficult to expose.

Bleeding also occurs from the collaterals between the surface of the liver and the diaphragm. As much as a litre of blood may be lost rapidly when the right coronary ligament is divided. This can first be controlled with packing and subsequently with a continuous running stitch of atraumatic catgut. Bleeding can also occur as a result of a coagulation defect. This should be prevented and adequate fibrinogen given if massive transfusion is needed. Fibrinolysis can take place during or after resection of the liver; hence epsilon aminocaproic acid should be available and used when the blood fails to clot. Bleeding from the intersegmental veins has led many surgeons to use hepatic clamps. We have not found this to be necessary.

References

HOU P. C. (1958) Malignant tumours of the liver, extrahepatic ducts and gall bladder. In: RAVEN R. W. *Cancer*, Vol. 2. London, Butterworths, pp. 168–185.

ISLAMI A. H., PACK G. T. and HUBBARD J. C. (1958) Regenerative hyperplasia of the cirrhotic liver following partial hepatectomy. *Cancer* **11**, 663–686.

LIN T. Y. (1966) The results of hepatic lobectomy for primary carcinoma of the liver. *Surg. Gynecol. Obstet.* **123**, 289–294.

LIN T. Y. (1973) Results of 107 hepatic lobectomies with a preliminary report on the use of a clamp to reduce blood loss. *Ann. Surg.* **177**, 413–421.

MCFADZEAN A. J. S., TODD D. and TSANG K. C. (1958) Polycythemia in primary carcinoma of the liver. *Blood* **13**, 427–435.

ONG G. B., CHU E. P. H., YU F. Y. K. and LEE T. C. (1965) Spontaneous rupture of hepatocellular carcinoma. *Br. J. Surg.* **52**, 123–129.

ONG G. B. and TAW J. L. (1972) Spontaneous rupture of hepatocellular carcinoma. *Br. Med. J.* **4**, 146–149.

PACK G. T. and MOLANDER D. W. (1960) Metabolism before and after hepatic lobectomy for cancer; studies in 23 patients. *Arch. Surg.* **80**, 685–692.

SMITH R. (1968) Personal communication.

STEWART M. J. (1931) Precancerous lesions of the alimentary tract. *Lancet* **2**, 617–622.

TULL J. C. (1932) Primary carcinoma of the liver: a study of 134 cases. *J. Pathol. Bact.* **35**, 557–562.

WANG C. E. and LI K. T. (1963) Surgical treatment of primary carcinoma of liver. *China Med. J.* **82**, 65–78.

Br. J. Surg. Vol. 62 (1975) 431–437

The effect of hepatic ischaemia on liver function and the restoration of liver mass after 70 per cent partial hepatectomy in the dog

R. J. MACKENZIE, C. M. FURNIVAL, MAUREEN A. O'KEANE
AND L. H. BLUMGART*

SUMMARY

Partial hepatectomy was performed in dogs either as the only procedure or following a period of ischaemia to the liver remnant produced by inflow occlusion for periods of 30–60 minutes before partial hepatectomy. Temporary portal decompression was maintained through the portion of liver subsequently excised.

1. Survival in dogs subjected to partial hepatectomy and ischaemia to the liver remnant was similar to that in animals after partial hepatectomy alone.

2. Metabolic changes were similar in both groups but dogs submitted to partial hepatectomy and ischaemia to the remnant had higher serum alkaline phosphatase and alanine amino-transferase levels with increased bromsulphthalein retention in the fourth to sixth postoperative weeks.

3. Replacement of liver mass proceeded rapidly in all groups of animals.

It is concluded that ischaemia of the liver remnant for up to 60 minutes preceding partial hepatectomy in the dog is consistent with survival and produces little change in postoperative liver function or in the rate of restoration of liver mass.

MAJOR hepatic resection, performed with increasing frequency for liver injury and liver cancer, is followed by metabolic and haematological changes which appear to be more marked in severely injured hypotensive patients (Vajrabukka et al., 1975). Hypoglycaemia, hypo-albuminaemia, jaundice and bleeding disorders are all known to occur after major liver resection, but the pattern of these disorders in relation to the condition of the liver and the general condition of the patient prior to operation has not been clearly defined.

It is almost impossible in the clinical stiuation to investigate the mechanisms underlying these changes because it is difficult to distinguish the effect of liver resection itself from the effects of preceding liver injury, other injuries and hypovolaemic shock. In order to investigate these problems the metabolic and haematological changes which follow major liver resection have been studied in the dog. In particular, the effect of various periods of normothermic ischaemia of the liver remnant prior to resection in relation to postoperative liver function and restoration of liver mass has been studied. The following report is concerned with the metabolic changes which follow hepatectomy in these circumstances.

Materials and methods

General methods

Experiments were performed on 39 dogs weighing 17·0–33·6 kg (mean 23·8 kg). Each animal was fasted for 18 hours before operation. After premedication with acetylpromazine (Acepromazine, Crookes Veterinary Ltd, 1 mg i.m.), anaesthesia was induced by intravenous sodium pentobarbitone (Intraval Sodium, May & Baker Ltd, 25 mg/kg), an endotracheal tube was passed and anaesthesia maintained with a mixture of nitrous oxide, halothane and oxygen with the animal breathing spontaneously. Catheters were placed in the right femoral artery and in the portal vein via the left gastric vein to record systemic arterial and portal venous blood pressures respectively. Each catheter was connected to a pressure transducer (Devices Instruments Ltd, Type 4-327-L221), and pressures were recorded continuously throughout the operative procedure on a multi-channel recorder (Devices Instruments Ltd, Model MX4). Each pressure-recording system was calibrated before and at intervals during each experiment. During the operation and in the immediate postoperative period, infusions of 0·9 per cent saline solution were given into the cephalic vein to replace blood loss and to maintain fluid balance. Measurements of pH, $Pa\text{CO}_2$ and $Pa\text{O}_2$ were made on samples of femoral arterial blood at intervals during the operation, and metabolic acidosis was corrected by intravenous injection of 8·4 per cent sodium bicarbonate solution.

Partial hepatectomy

Partial hepatectomy was carried out by a modification of the method described by Sigel (1963), in which the left and central portions of the liver are removed, leaving the right lateral and caudate lobes as the liver remnant (*Fig.* 1). Through a midline upper abdominal incision the gastrohepatic omentum is divided and the branches of the bile duct, hepatic artery and portal vein to the left and central parts of the liver are ligated and divided. The left and central hepatic veins are secured between clamps, divided and oversewn. Partial hepatectomy is completed by ligation and division of the papillary process, leaving a minimum of crushed liver tissue, namely a few grammes adjacent to the

---

* University Department of Surgery, Royal Infirmary, Glasgow, and Wellcome Surgical Research Institute, University of Glasgow.

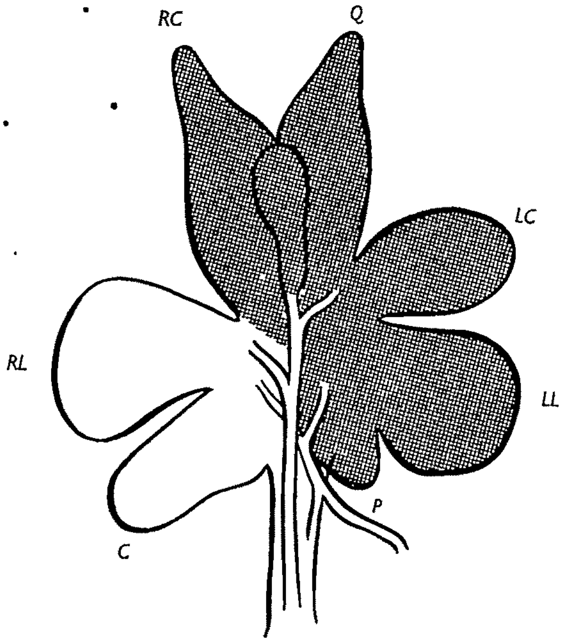


Fig. 1. Canine liver: *C*, caudate lobe; *RL*, right lateral lobe; *RC*, right central lobe; *Q*, quadrate lobe; *LC*, left central lobe; *LL*, left lateral lobe; *P*, papillary lobe. The shaded area represents the portion removed during the procedure of 70 per cent partial hepatectomy and is that part through which portal decompression was achieved during inflow occlusion of the right lateral and caudate lobes.

Table I: METHODS USED FOR SERUM BIOCHEMICAL ESTIMATIONS

Bilirubin	Boehringer* Test Pack
Alkaline phosphatase	Boehringer Test Pack
SGPT and SGOT	Boehringer Test Pack
Total protein	Biuret method
Albumin	A modification of the bromcresol green dye method (McPherson and Everard, 1972)
BSP	Dose of 5 mg/kg; one blood sample at 30 minutes (Kaneko and Cornelius, 1970)
Blood sugar	Boehringer Test Pack

* The Boehringer Corp. (London) Ltd, Bilton House, Uxbridge Road, Ealing, London W5.

ligature around the papillary process. This technique removes 70 ± 5 per cent of the liver substance (Sigel, 1963).

The excised liver was weighed after removing the gallbladder and draining excess blood. After completion of the procedure, the catheter in the femoral artery was removed and the artery repaired, the portal cannula was removed and the left gastric vein tied and the abdominal wound was closed. Six weeks after operation each animal was sacrificed and the liver remnant removed and weighed. Restoration of liver mass was measured by expressing the weight of the liver remnant post mortem as a percentage of the estimated total liver weight prior to resection. Estimated total liver weight was derived from the weight of the liver resected at the partial hepatectomy on the assumption that this represented 70 per cent of the liver mass (Sigel, 1963). Samples of tissue were taken from the liver resected at partial hepatectomy and from the regenerated liver remnant post mortem for histological examination.

Temporary inflow occlusion of liver remnant
In 17 animals, after division of the bile ducts and the branches of the hepatic artery to the central and left lobes, the branches of the portal vein and hepatic artery supplying the liver remnant, i.e. caudate and right lateral lobes, were occluded for periods of 30, 45 or 60 minutes. At the end of each period, after re-establishing inflow to the liver remnant, partial hepatectomy was performed as described above. The efficacy of this complete inflow block was tested by an isotope clearance method, injecting ^{133}Xe (3 µl; 10 µCi/ml) into the substance of the remnant, with a scintillation counter (Rank Precision Industries, Type P 1062) placed over the injection site; activity was recorded using a ratemeter (Nuclear Enterprises, Type 7000 Series) and chart recorder (Servoscribe, Type RE 511.20). Intralobar temperature was recorded from a thermistor probe placed within one of the remaining lobes. During the period of occlusion, portal venous blood drained freely through the lobes of the liver later to be excised.

Liver function tests
Serum bilirubin, alkaline phosphatase, alanine transaminase (SGPT), aspartate transaminase (SGOT), total protein, albumin and bromsulphthalein (BSP) retention were measured daily in the first week after operation and at weekly intervals up to 6 weeks. Blood sugar was measured in the early postoperative phase. The methods used to estimate each of these substances are shown in *Table I.*

Experimental groups
The following groups of experiments were performed:

Group I: Control animals (5 dogs); laparotomy alone (including handling of abdominal viscera), with anaesthesia for a time similar to that in animals undergoing partial hepatectomy.

Group II: Partial hepatectomy alone (17 dogs).

Group III: Partial hepatectomy following a period of total inflow occlusion of the liver remnant for 30–60 minutes with concomitant portal decompression (17 dogs).

Results

General

In the initial experience of hepatectomy 2 animals died as a result of technical error. In subsequent experiments obstructive jaundice followed hepatectomy in 3 animals. In each case this was shown to be due to accidental ligation of the bile duct draining the liver remnant, associated with an anatomical variation in the biliary system. In later experiments animals found to have this variation were excluded from the resection programme and used as controls. During the procedures described in detail below, systemic arterial pressure ranged from 170/115 to 80/55 mm Hg (mean

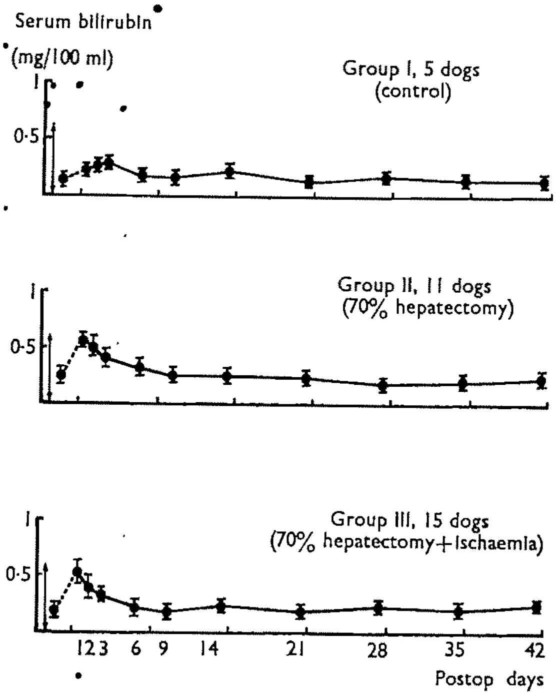


Fig. 2. Total serum bilirubin levels (mean ±1 s.e.) in groups I, II and III.

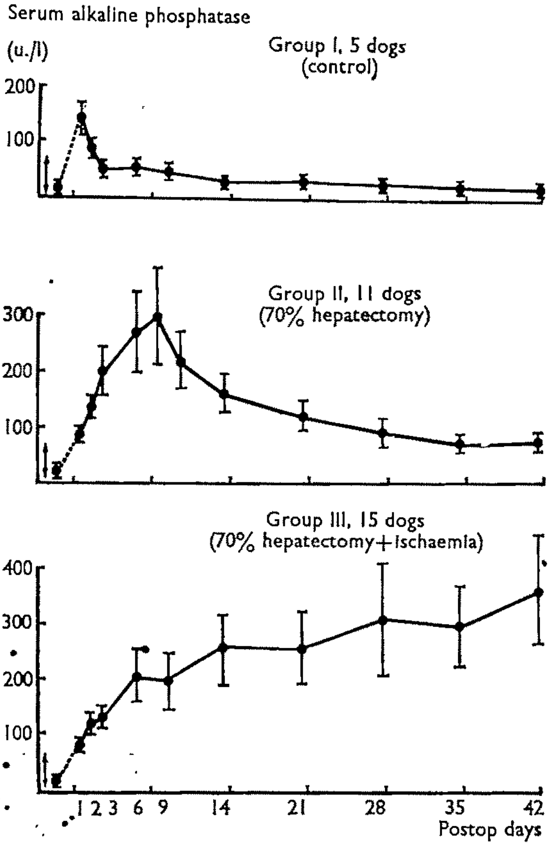


Fig. 3. Serum alkaline phosphatase levels (mean ±1 s.e.) in groups I, II and III.

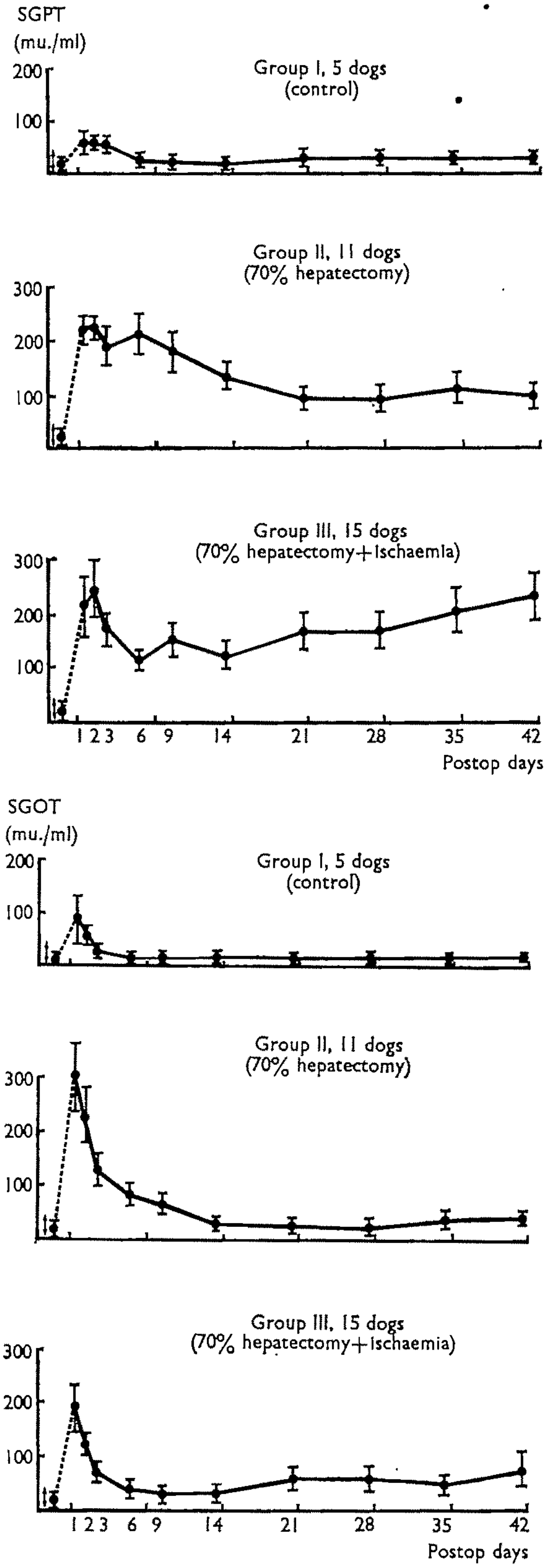


Fig. 4. SGPT and SGOT levels (mean ±1 s.e.) in groups I, II and III

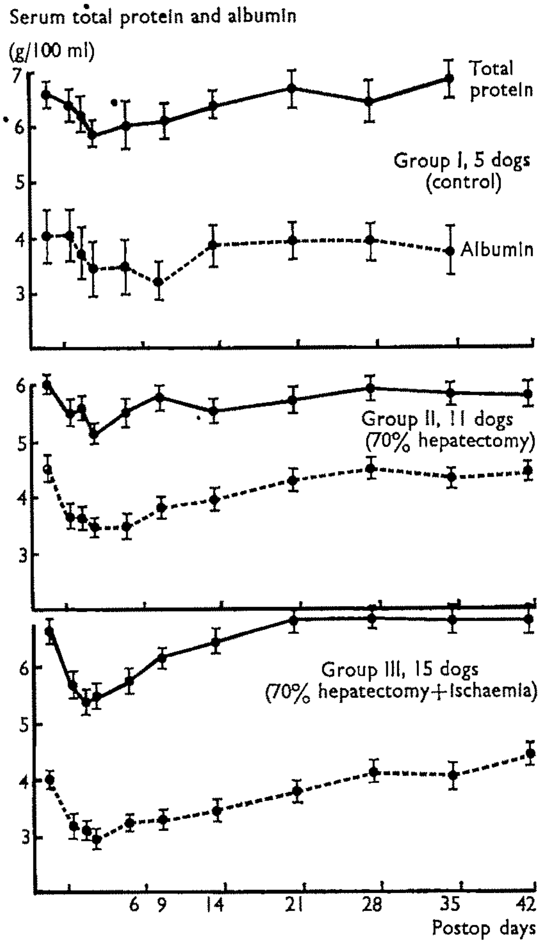


Fig. 5. Total serum protein and serum albumin levels (mean ±1 s.e.) in groups I, II and III.

126/84 mm Hg). Portal venous pressure was 3·4–19·0 cm H_2O (mean 10·4 cm H_2O) prior to resection; following resection, portal venous pressure increased by 1–8 cm H_2O, a mean increase of 3·0 cm H_2O. In all the experiments the initial arterial blood pH was 7·16–7·3 (mean 7·24) and the lowest value during the experiment was 7·08–7·27 (mean 7·23). Arterial blood gases were recorded throughout each experiment; the range of values was for Pa_{O_2} 97–192 mm Hg (mean 149 mm Hg), and for Pa_{CO_2} 37–68 mm Hg (mean 52 mm Hg).

Surviving animals tolerated the procedures well and were ambulant and drinking on the day after operation. They had resumed a full diet by the third postoperative day and maintained their weight. None showed an overt bleeding tendency in the postoperative period nor did hypoglycaemia (i.e. less than 40 mg/100 ml) occur.

Group I

In dogs undergoing laparotomy alone (i.e. control animals) no important change in serum bilirubin was found (*Fig.* 2), and the serum alkaline phosphatase showed a small transient rise with a maximum on the first postoperative day (*Fig.* 3). No important change in SGPT was found, but serum SGOT rose on the first postoperative day to a mean value of 99 mu./ml (range 43–235 mu./ml), returning to normal values before the end of the first week (*Fig.* 4). A reduction in total protein was due to a fall in serum albumin, reaching a minimum value at the end of the first week after operation (mean 34 g/l, range 26–41 g/l); preoperative values were obtained by the end of the second week as shown in *Fig.* 5.

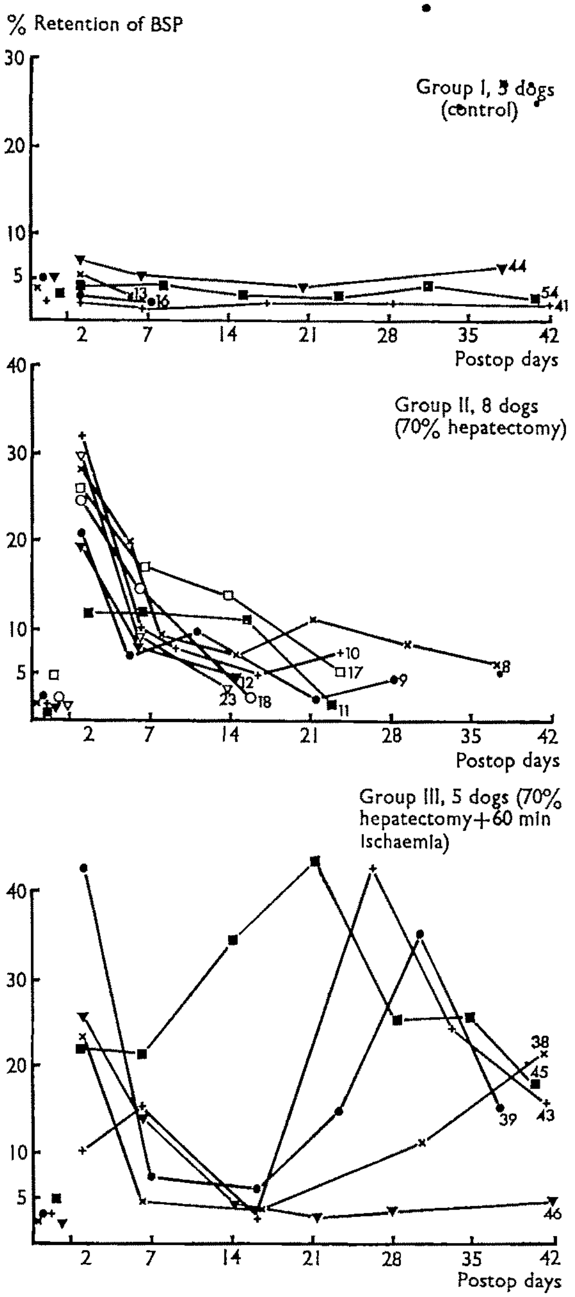


Fig. 6. BSP clearances from animals in groups I and II and after 60 minutes' ischaemia in group III. Each animal's results are shown separately.

On the second postoperative day BSP retention was less than 7·5 per cent at 30 minutes in 5 animals tested (*Fig.* 6).

Group II

Of 17 animals undergoing partial hepatectomy alone, 2 died from technical failure during hepatectomy (*see above*). Of the remaining 15 dogs, 14 (93 per cent) survived for 6 weeks after hepatectomy. The dog which died recovered from anaesthesia but failed to drink and died on the third day after operation. No clear cause of death was established. Of the 14 survivors, 3 developed obstructive jaundice as described above; these were excluded from the analysis, and the biochemical tests described below were performed on the remaining 11 dogs.

Measurements of serum bilirubin in these dogs showed a small transient rise (mean 0·6 mg/100 ml, range 0·27–1·04 mg/100 ml) in the first 3 days after operation; the mean maximum did not exceed the upper limit of normal (*Fig.* 2). Serum alkaline phosphatase showed a much greater rise to a peak (mean 290 u./l, range 100–624 u./l) at the end of the first week. In the remaining 5 weeks the alkaline phosphatase decreased gradually, the mean at 6 weeks being at the upper limit of normal values (mean 70 u./l, range 23–162 u./l), as shown in *Fig.* 3.

Both SGOT and SGPT showed a large early increase after partial hepatectomy (*Fig.* 4). In each case the peak occurred within 48 hours of operation (SGOT mean 300 mu./ml, range 100–627 mu./ml; SGPT mean 220 mu./ml, range 116–342 mu./ml). Both enzymes returned towards normal values which were reached in the case of SGOT by the third week after operation but SGPT remained persistently elevated at 6 weeks (mean 100 mu./ml, range 21–242 mu./ml).

Changes in serum total protein paralleled those of serum albumin (*Fig.* 5), which fell to its lowest value (mean 35 g/l, range 29–38 g/l) in the first week after operation, returning thereafter to preoperative levels in the sixth week (mean 44 g/l, range 38–49 g/l).

Retention of BSP was measured in 8 of the 14 dogs surviving partial hepatectomy alone and showed an early rise to abnormal values on the second postoperative day (mean 25 per cent, range 12–32 per cent). Subsequent measurements showed a return towards preoperative values, retention being less than 10 per cent in all animals by the fourth week after operation (*Fig.* 6).

Restoration of liver mass was measured as described above, and in this group was a mean of 91 per cent (range 76–112 per cent) at the time of sacrifice. Histological examination of liver taken from these animals at post-mortem showed a pattern indistinguishable from that of a normal dog liver.

Group III

Of 17 dogs in which the vascular supply to the liver remnant (caudate and right lateral lobes) was completely occluded for periods of 30–60 minutes (*Table II*), 15 dogs (88 per cent) survived. Neither of the 2 dogs which died regained consciousness after anaesthesia and the cause of death was not established. The period of inflow occlusion in these 2 dogs was 45 and 60 minutes.

Table II: TIME OF OCCLUSION AND SURVIVAL OF ANIMALS IN GROUP III

Time of occlusion (min)	No. of animals	Survivors
30	5	5
45	6	5
60	6	5

Serum bilirubin in this group showed only a small rise (mean 0·6 mg/100 ml, range 0·31–1·04 mg/100 ml) in the first 3 days after operation, and the mean maximum did not exceed the upper limit of normal (*Fig.* 2). Serum alkaline phosphatase was elevated in the immediate postoperative period (mean 130 u./l, range 53–262 u./l), but in some animals continued to rise slowly throughout the period of survival (*Fig.* 3), the highest mean values being recorded 6 weeks after operation (mean 360 u./l, range 49–940 u./l).

There was a large early rise in SGOT and SGPT to a peak about 48 hours after partial hepatectomy (SGOT mean 190 mu./ml, range 80–656 mu./ml; SGPT mean 250 mu./ml, range 85–858 mu./ml). Both enzymes subsequently returned towards normal values (*Fig.* 4), but whereas SGOT was within the normal range 2 weeks after operation, SGPT remained elevated, the mean remaining consistently about 100 mu., and in the fifth and sixth weeks after hepatectomy showed a secondary rise reaching at 6 weeks a peak similar to that found 48 hours after operation (mean 230 mu./ml, range 21–628 mu./ml). The serum total protein in these dogs fell in the early postoperative period due to the fall in serum albumin which reached its lowest value (mean 29 g/l, range 22–36 g/l) on the third day after the operation (*Fig.* 5), thereafter gradually returning to a mean value slightly in excess of the preoperative value.

The BSP test showed a variable pattern in dogs after partial hepatectomy preceded by inflow occlusion. All 15 dogs had an early increase in retention (mean 24 per cent, range 11–43 per cent on the second postoperative day). In 5 dogs after 30 minutes of ischaemia the changes were essentially similar to those in group II animals. However, in the other 10 dogs after ischaemia for 45 or 60 minutes 7 animals showed a late rise to between 12 and 42 per cent retention at various times between the third and sixth weeks. In 4 of these dogs the tendency was a return towards normal values after this late rise, but in 2 animals a progressive elevation was recorded and in another dog a third increase occurred in the fifth and sixth weeks. The changes in the animals after 60 minutes' ischaemia are illustrated in *Fig.* 6.

Restoration of liver mass in these dogs showed a mean of 83 per cent (range 76–100 per cent) of the estimated preoperative weight.

Discussion

The main purpose of the investigation was to examine the changes in liver function which occur in partially hepatectomized animals in whom the liver remnant has suffered a period of ischaemia prior to hepatectomy. In severe hypovolaemic shock in human subjects, hypoperfusion of the liver may contribute to liver damage resulting in impairment of liver function after partial hepatectomy; recently, doubt has been cast on the release of endotoxin into the portal circulation as an important mechanism in prolonged hypovolaemic shock in man (Herman et al., 1974), and although other toxic substances may exist in blood from a hypoperfused gut, the effect of ischaemia itself on the liver requires further definition.

Perhaps the most important conclusion from these experiments is that ischaemia of the liver remnant for up to 1 hour is compatible with survival in the dog. None of the major problems encountered in clinical practice, including severe hypoglycaemia and coagulation defects, was seen in these animals. No comparable series of ischaemia to the liver remnant has been reported, but the overall survival rate of 88 per cent with 83 per cent surviving 60 minutes of inflow block and subsequent 70 per cent hepatectomy is better than that of 50–60 per cent survival reported after 60 minutes' inflow block to the whole liver with portal diversion (Farkouh et al., 1971).

There is no doubt that ischaemia was complete in these experiments since this was confirmed by the ^{133}Xe clearance method. It is possible that portal decompression by diversion through the lobes subsequently resected and also the increased rate of flow through the remnant after hepatectomy contributed considerably to this high survival rate.

Examination of measurements made in control animals shows that only minor changes in the biochemical tests of liver function occur after laparotomy alone. The more severe changes in liver function tests found after 70 per cent hepatectomy alone establish a pattern of biochemical changes including an increase in serum alkaline phosphatase and transaminase together with a fall in serum albumin; these changes show a return towards normal values during the period of survival. Similarly, an abnormal increase in BSP retention occurs only in the early postoperative period. These findings substantiate those of previous studies (Aronsen and Ericsson, 1968; Flatmark et al., 1973) with only small differences. One of the surprising features in this and other studies is the small increase in serum bilirubin which returns to preoperative levels within the first week after hepatectomy. We have not found a peak value occurring later in the postoperative period (3 weeks), as described by Flatmark et al. (1973) in dogs undergoing hepatectomy alone.

As an index of the synthetic function of the liver, the fall in serum albumin takes some weeks to recover and indicates impairment of this aspect of liver function. The changes recorded are similar to those reported by Aronsen and Ericsson (1968) after 35–60 per cent partial hepatectomy.

Animals in which the liver remnant was rendered ischaemic were treated as a single group for analysis of liver function tests although the period of ischaemia ranged from 30 to 60 minutes; a relatively small number of animals justifies this method. In comparing the effects in this group with those which follow hepatectomy alone, the most striking differences are in the alkaline phosphatase and SGPT. The progressive increase in alkaline phosphatase is in sharp contrast to the steady return towards normal values which characterizes a straightforward partial hepatectomy. The reasons for this are obscure since in these animals the absence of a sustained rise in bilirubin excludes major excretory obstruction as a cause. Also opposing obstruction as an explanation for the escalating alkaline phosphatase is the normal BSP retention in some animals in the later postoperative period. There is certainly no clear correlation between a late rise in alkaline phosphatase and abnormal BSP retention, although these two features were concurrent in the majority of animals.

In the present study proliferation of hepatoctyes after hepatectomy (i.e. 'regeneration') was not studied; the major changes in mitosis and in DNA synthesis are known to occur soon after hepatectomy and are over by the sixth postoperative week. However, the end result of regeneration, regrowth of the liver towards its preoperative weight referred to here as 'restoration of liver mass', was measured in each hepatectomized animal. The remarkable capacity for regrowth was evident in both experimental groups, but a comparison of liver weights shows that the restoration of liver mass was slightly less at 6 weeks (83 per cent) after ischaemia than after hepatectomy alone (91 per cent). Although this difference is statistically significant, there is considerable overlap in the individual measurements which comprise these groups. It is therefore reasonable to conclude that in terms of liver weight no important effect is found 6 weeks after ischaemia of up to 60 minutes' duration.

In conclusion, these results cast doubt on the belief that the liver is extremely sensitive to short periods of ischaemia, although in this case the observations have been made on the dog liver, in contrast to the majority of observations made on the pig liver. Studies related to transplantation have suggested that 'warm ischaemia time' (which is analogous to the period of normothermic ischaemia in our animals) must be less than 30 minutes to ensure survival (Peacock et al., 1969), although it may be said that the procedure of transplantation, together with any immune reaction, is an additional stress for the organ in that situation. Battersby et al. (1974) have recently confirmed that the pig liver can withstand total normothermic ischaemia of 30 minutes if portal diversion is incorporated, and interestingly have shown by transhepatic sampling in the acute phase of ischaemia the initiation of elevated alkaline phosphatase and transaminase which we have demonstrated in the later period of survival.

In relation to liver resection which was the prime purpose of this study it is interesting to find that the restoration of liver mass is not severely impaired by a period of complete ischaemia. Initial results from a study of more prolonged ischaemia (currently in progress) show that hypoglycaemia and major coagulation abnormalities do occur in the dog in these circumstances and are accompanied by a significantly higher mortality. There may therefore be a very narrow margin between preservation of function, including the ability of the liver to regenerate, and failure of function resulting in death of the animal. From these experiments it appears that the critical period of total ischaemia in the dog is not less than 60 minutes.

Acknowledgements

One of us (R. J. M.) was in receipt of a Wellcome Surgical Research Fellowship.

This work was supported by a grant from the Scottish Home and Health Department.

References

ARONSEN K. F. and ERICSSON B. (1968) Metabolic changes following partial hepatectomy in dogs. *Acta Chir. Scand.* **134**, 282–286.

BATTERSBY C., HICKMAN R., SAUNDERS S. J. and TERBLANCHE J. (1974) Liver function in the pig: 1. The effects of 30 minutes' normothermic ischaemia. *Br. J. Surg.* **61**, 27–32.

FARKOUH E. F., DANIEL A. M. and MACLEAN L. D. (1971) The effect of collateral circulation on survival in liver ischaemia. *J. Surg. Res.* **11**, 130–134.

FLATMARK A., RO J. S., JAKOBSEN A., ENGE I. and SKREDE S. (1973) Regeneration and metabolic changes following extensive liver resection in dogs. *Scand. J. Gastroenterol.* **8**, 609–613.

HERMAN C. M., KRAFT A. R., SMITH K. R., ARTNAK E. J., CHISHOLM F. C., DICKSON L. G., MCKEE A. E., HOMER L. D. and LEVIN J. (1974) The relationship of circulating endogenous endotoxin to haemorrhagic shock in the baboon. *Ann. Surg.* **179**, 910–916.

KANEKO J. J. and CORNELIUS C. E. (ed.) (1970) *Clinical Biochemistry of Domestic Animals*, 2nd ed., vol. I. London, Academic Press.

MCPHERSON I. G. and EVERARD D. W. (1972) Serum albumin estimation: modification of the bromcresol green method. *Clin. Chim. Acta* **37**, 117–121.

PEACOCK J. H., IMMELMAN E. J., HOBBS K. E., MITRA S. K., BOWES J. B. and HUNT A. C. (1969) Experimental appraisal of factors involved in provision of donors. *Br. Med. J.* **1**, 349–352.

SIGEL B. (1963) Partial hepatectomy in the dog. *Arch. Surg.* **87**, 788–791.

VAJRABUKKA T., BLOOM A., SUSSMAN M., WOOD C. B. and BLUMGART L. H. (1975) Postoperative problems and management after hepatic resection for blunt injury to the liver. *Br. J. Surg.* **62**, 189–200.

Br. J. Surg. Vol. 62 (1975) 438–440

Orthotopic liver transplantation utilizing a vascular stapling instrument

P. T. BARRON, I. J. VOGELFANGER AND W. G. WADDELL*

SUMMARY

A technique of orthotopic liver transplantation in the pig is described in which the main feature is the accomplishment of four of the five anastomoses by the use of the Vogelfanger NRC vascular suturing instrument. The advantage of this instrument is the rapid accomplishment of safe leak-proof anastomoses.

DESCRIPTIONS of orthotopic liver transplantation in the pig have been reported by many authors (Garnier et al., 1965; Cordier et al., 1966; Mieny et al., 1967; Terblanche et al., 1967; Calne et al., 1968; Chalstrey et al., 1971). The surgical technique is of critical importance. The incidence of complications is frequent and often fatal. The most dangerous period is that interval during implantation of the donor liver when the recipient animal is totally bereft of liver function. It is vital, therefore, to restore hepatic blood supply promptly, and if this anhepatic period is prolonged beyond 45 minutes serious and often irreversible metabolic acidosis occurs. The usefulness and versatility of the Canadian Vogelfanger NRC vascular stapler (Vogelfanger et al., 1962, 1967) suggested an application to liver transplantation where rapidity in the performance of the vascular anastomoses is so desirable. The use of this instrument and modifications in the operative technique are described.

Materials and methods

Pigs of differing breeds, White Landrace and Black Poland China, of approximately 30 kg were used.

Donor

Through a subcostal incision the donor liver was freed from all its ligamentous attachments, and the portal vein, hepatic artery and common bile duct were dissected to the superior border of the pancreas.

The subhepatic vena cava was isolated down to the renal vein, avoiding injury to the suprarenal vessels. The triangular ligaments above the liver were divided and phrenic veins draining into the suprahepatic inferior vena cava ligated. The liver was cooled *in situ* through the portal vein with Ringer's lactate solution containing 10 ml of 8·4 per cent sodium bicarbonate, 200 mg of lidocaine, 1 ml of heparin and 100 mg of hydrocortisone per litre. Hepatectomy was then performed, preserving as much of the donor vessels as possible.

Recipient

The following parameters were monitored: arterial pressure, central venous pressure, temperature, ECG and serial estimations of $P\text{CO}_2$ and standard bicarbonate. Hepatectomy was performed in the same manner as in the donor. On a number of occasions it was necessary to ligate the gastroduodenal artery but no damage to the duodenum was observed. Portosystemic shunt was performed by cannulation from the splenic to the jugular vein following splenectomy. Heparinization was performed with 0·5 mg of heparin per kg. The donor liver was implanted into the recipient and the anastomoses done in the following order: suprahepatic vena cava, portal vein, hepatic artery, infrahepatic vena cava and common bile duct. The suprahepatic inferior vena cava anastomosis was done as a single layer continuous suture utilizing 3/0 silk. End-to-end anastomoses between the donor and recipient portal vein, hepatic artery, subhepatic inferior vena cava and common bile duct were performed with the Vogelfanger NRC vascular stapling instruments (Vogelfanger et al., 1962, 1967), Mark IV (handling vessels 2–5 mm in diameter) and Mark XII (for vessels 6–12 mm in diameter).

The key components of the vascular staples are the stapling bushing with the U-shaped tantalum staples and a corresponding anvil bushing with appropriately shaped moulding surfaces to bend the staples (*Fig.* 1).

The vessel diameters were first measured. Vessel size ranged from 10 to 12 mm for the portal vein and subhepatic inferior vena cava, and from 2 to 3 mm for the hepatic artery. The diameter of the common bile duct was approximately 5–6 mm.

Cuffs of donor and recipient vessels were then everted over the driving and anvil bushings respectively and held in position by plastic rings (*Figs.* 2, 3). In the larger vessels this was done by hand, and in the hepatic artery was readily achieved by an everting instrument. The two handles were locked together and the staple-driving mechanism operated to drive the staples through the vessel wall, towards the anvil bushing, moulding the driven staples in the shape of a letter B, thus forming an interrupted mattress suture. Removal of the instrument left a stapled vascular anastomosis.

When the portal anastomosis was completed the vascular clamp was removed and the liver perfused with 300–400 ml of portal venous blood which was allowed to egress into the abdominal cavity through the infrahepatic vena cava. In the preceding few

---

* Department of Surgery, University of Ottawa, and Ottawa Civic Hospital, Ottawa, Ontario, Canada.

Requests for reprints to I. J. Vogelfanger, Chief, Division of Surgical Research, Ottawa Civic Hospital, 1053 Carling Avenue, Ottawa, Ontario, Canada K1Y 4E9.

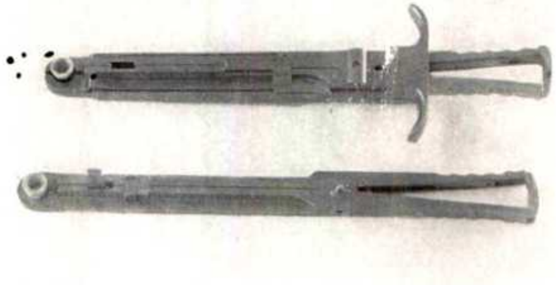


Fig. 1. Instrument disassembled.

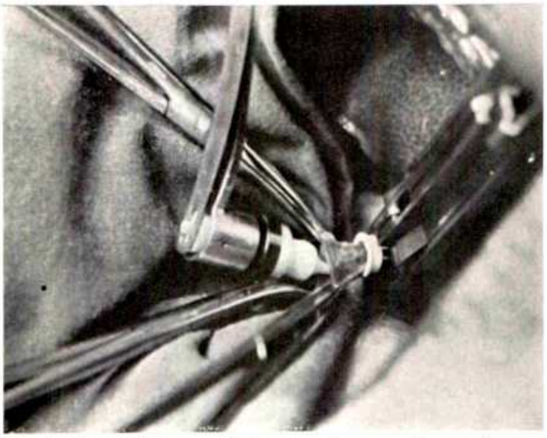


Fig. 2. Evertor being applied to produce a cuff over the bushing of the closed instrument.

minutes the animal had been transfused with a unit of blood to allow for this loss. The subhepatic inferior vena cava was then clamped and the vascular clamps on the suprahepatic inferior vena cava were removed to restore portal to systemic circulation. The remaining anastomoses including the common duct were then completed rapidly, utilizing the same technique (*Fig*. 4).

The time taken to complete the three critical anastomoses—suprahepatic vena cava, portal vein and hepatic artery—was approximately 15–20 minutes using this technique.

Prior to closure of the abdomen and neck, vagotomy and pyloromyotomy were done (Calne et al., 1968).

Discussion

The complexities of liver transplantation relate to technical problems, the susceptibility of the liver to ischaemia and the tendency of the animal to develop serious metabolic problems during the anhepatic period. For this reason the ischaemic interval for the graft and the anhepatic period in the recipient should be as short as possible. A functioning portosystemic circulation is achieved quickly by first completing the suprahepatic vena cava anastomosis and then the portal vein, and immediately allowing a flow through the liver. The use of the Vogelfanger NRC vascular stapling instrument allows the rapid completion of these anastomoses, and in our hands shortens the anhepatic time to under 15 minutes. The hepatic artery and infrahepatic vena cava anastomoses may then be equally rapidly completed, allowing the total time for the vascular anastomoses to be under 45 minutes.

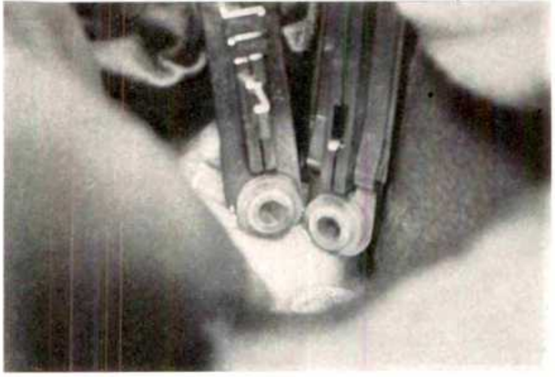


Fig. 3. Both cuffs everted with nylon rings left by the evertor for fixation of the cuffs. Handles ready for assembly.

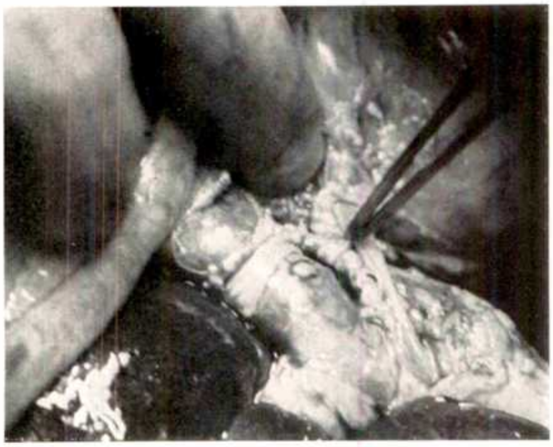


Fig. 4. Completed anastomosis of the portal vein (left), hepatic artery (right) and common duct (above the hepatic artery).

The instrument gives a very precise intima to intima leak-proof anastomosis with a high degree of long term patency (Vogelfanger et al., 1962, 1967). A small vessel anastomosis with this technique also minimizes the trauma to the liver consequent upon dissection of the hepatic artery down to the coeliac artery and aorta which is necessary when a larger vascular reconstruction is done.

A series of 31 liver transplants was done utilizing this method, with an operative mortality of 7 and with 12 animals surviving for 6–160 days.

References

CALNE R. Y., YOFFA D. E., WHITE H. J. O. and MAGINN R. R. (1968) A technique of orthotopic liver transplantation in the pig. *Br. J. Surg*. **55**, 203–206.

CHALSTREY L. J., PARBHOO S. P., TAPPIN A., BAKER G. J., GRACEY L. R. H., MULLEN P. A. and LESTER R. (1971) Technique of orthotopic liver transplantation in the pig. *Br. J. Surg*. **58**, 585–588.

CORDIER G., GARNIER H., CLOT J. P., CAMPLEZ R., GORIN J. P., CLOT P., RASSINIER J. P., NIZZA A. and LEVY R. (1966) La greffe de foie orthotopique chez le porc. Premiers résultats. *Mém. Acad. Chir.* **92**, 799.

GARNIER H., CLOT J. P., BERTRAND M., CAMPLEZ P., KUNLIN A., GORIN J. P., LEGOAZIOU F., LEVY R. and CORDIER G. (1965) Greffe de foie chez le porc: approche chirurgicale. *C.R. Acad. Sci.* (*D*) (*Paris*) **260**, 5621–5623.

MIENY C. J., MOORE A. R., HOMATAS J. and EISEMAN B. (1967) Homotransplantation of the liver in pigs. *S. Afr. J. Surg.* **5**, 109–114.

TERBLANCHE J., PEACOCK J. H., BOWES J., DAVIES R. P., TIERRIS E. J., PALMER D. B. and HUNT A. C. (1967) The technique of orthotopic liver transplantation in the pig. *Br. J. Surg.* **54**, 231.

VOGELFANGER I. J., BEATTIE W. G. BROWN F. N., DEVITT J. E., SCOBIE T. K. and SCOBIE D. H. (1962) The problem of small vessel anastomosis. *Surgery* **52**, 354–362.

VOGELFANGER I. J., IRVINE A. H. and COLLINS W. E. (1967) Experimental orthotopic kidney transplantation. *Can. J. Surg.* **10**, 223–227.

Br. J. Surg. Vol. 62 (1975) 441–443

Effect of surgical trauma on plasma concentrations of cyclic AMP and cortisol

G. V. GILL, K. PRUDHOE, D. B. COOK AND A. L. LATNER*

SUMMARY

The response of plasma cortisol and cyclic AMP concentrations to surgical trauma was examined in 7 general surgical patients. Five patients made uncomplicated recoveries and showed peak cortisol levels at 6 hours postoperatively, returning to normal by 24 hours. One patient developed postoperative pneumonia and the plasma cortisol remained elevated up to 48 hours, and the final patient showed no cortisol response at all. The plasma cyclic AMP concentrations showed a consistent rise during the operation itself, which was statistically significant when compared with preoperative levels ($P<0{\cdot}0125$). Concentrations had fallen to normal by 6 hours in all the cases, except in the patient who developed pneumonia, where the plasma cyclic AMP also showed a prolonged elevation. The significance of these findings requires further elucidation, but the temporal relationship of the cyclic AMP and cortisol peaks would support the hypothesis that cyclic AMP may play a part in the mediation of ACTH release following surgical trauma.

THE intracellular role of cyclic AMP (adenosine 3′,5′-monophosphate) as a mediator of hormone action is well established (Robison et al., 1971). Recently, however, improved assay techniques have enabled cyclic AMP to be demonstrated in human plasma (Kaminsky et al., 1970). The function, if any, of this free extracellular nucleotide is at present uncertain, but preliminary work suggests that its concentration is at least to some extent hormone-dependent. Thus the intravenous infusion of high doses of glucagon (Broadus et al., 1970) and parathormone (Kaminsky et al., 1970) into healthy human subjects is associated with raised plasma cyclic AMP concentrations.

In order to examine the role of cyclic AMP in more physiological hormonal responses we have studied plasma cyclic AMP levels in relation to the cortisol response to surgical operation. Our results indicate significant elevations in plasma cyclic AMP concentrations during surgery, and this increase precedes the peak postoperative plasma cortisol elevation.

Patients and methods

Subjects were drawn from general surgical units. Patients with known endocrine diseases or undergoing only minor surgery were excluded; otherwise selection was completely random. Seven patients were studied. Blood samples were taken preoperatively (usually the morning of surgery), peroperatively (half-way through the operation), 6 hours postoperatively (timing from the beginning of surgery) and 24 hours and finally 48 hours after operation. Blood was taken from an antecubital vein with minimal venestasis, collected in heparinized tubes, immediately centrifuged at 4 °C, the plasma separated and then deep frozen at −20 °C. Plasma cortisol was measured by the competitive protein-binding method of Murphy (1967), adapted for ultramicro use by using dog plasma as the source of corticosteroid-binding globulin. Plasma cyclic AMP was also measured by a protein-binding technique (Latner and Prudhoe, 1973) developed from the method of Brown et al. (1971). The normal range for the plasma assay was 12–20 nmol/l.

Results

There were three types of cortisol response observed in the 7 patients.

1. '*Normal responders*'

Five patients underwent successful surgery and made an uncomplicated postoperative recovery. These subjects showed what may be called a 'normal' cortisol response, with levels peaking at 6 hours postoperatively and being almost back to normal by 24 hours (Johnston, 1972). The plasma cyclic AMP response in each of these patients was at its peak in the peroperative sample and had almost returned to normal by 6 hours after surgery. These results are shown in *Fig*. 1, and it will be seen that the responses are statistically significant.

2. '*Prolonged responders*'

It is known that high cortisol levels may persist after surgery if complications ensue (Birke et al., 1957). One patient in our series developed postoperative pneumonia, and the prolonged cortisol response is shown in *Fig*. 2. The plasma cyclic AMP level also remained elevated.

3. '*Non-responders*'

It has been known for some time that about 20 per cent of surgical patients show little or no cortisol response to operation (Thomasson, 1959; Espiner, 1966). In the present series 1 patient (who in fact underwent a combined rectal excision) showed this phenomenon, although a peroperative plasma cyclic AMP rise was again demonstrated (*Fig*. 3).

Discussion

The elevation of plasma cortisol concentration following surgical trauma is mediated by corticotrophin (ACTH), as shown by Ichikawa et al. (1971). The work of Hume et al. (1962) suggested that afferent nervous impulses from traumatized tissue to the

---

* Department of Clinical Biochemistry, University of Newcastle upon Tyne.

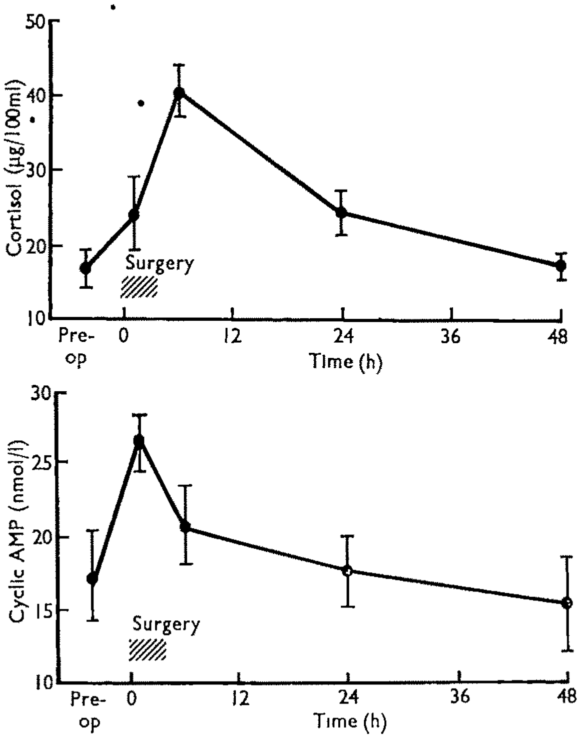


Fig. 1. Mean cortisol and cyclic AMP response (±standard error) to surgery in 5 patients. The differences between the preoperative and 6-hour levels of cortisol and between the pre- and peroperative levels of cyclic AMP are significant (0·0125>P>0·010).

hypothalamus stimulated ACTH release, but more recently it has been shown that animals with denervated pituitary glands can show a cortisol response to stress (Greer, 1970; Witorsch and Brodish, 1972), suggesting that a humoral factor or factors must exist. Cyclic AMP has been shown *in vivo* to elevate plasma cortisol levels, both in piglets (Cook et al., 1974) and in man (Angeli et al., 1973). The work in piglets has shown that the primary action of cyclic AMP is to stimulate ACTH release from the pituitary, and also that this action is shared by adenosine and other adenine nucleotides (Cook et al., 1974, 1975). As long ago as 1950 Green and Stoner provided evidence that release of adenine compounds into the circulation could mediate the cardiovascular response to trauma. They also provided some evidence that these compounds may be involved in the adrenocortical response to trauma (Stoner and Green, 1950).

Our results are consistent with the hypothesis that cyclic AMP (and possibly other compounds of adenine) exert a humoral action in the homeostatic responses to surgical trauma. The plasma cyclic AMP levels were at a peak before those of cortisol in each case. In the 1 patient who developed complications the plasma cyclic AMP remained elevated, as did the plasma concentration. The 'non-responder' showed a normal cyclic AMP peak during surgery, and thus may have an 'end organ failure' of cyclic AMP stimulation.

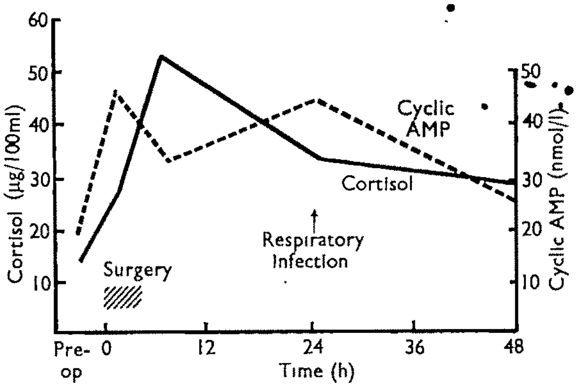


Fig. 2. Prolonged cortisol and cyclic AMP response to surgery in a patient developing a postoperative respiratory infection.

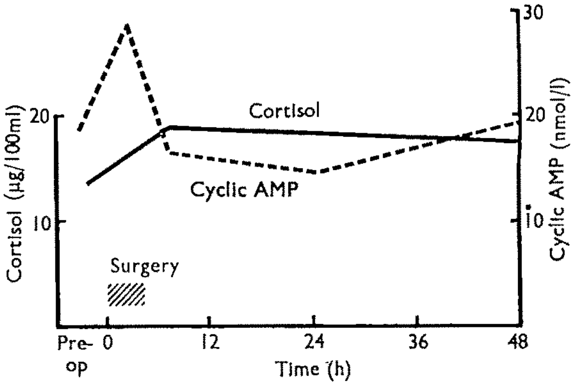


Fig. 3. Absence of cortisol response with a normal rise in cyclic AMP in a patient undergoing a combined rectal excision.

An intriguing problem is the source of the elevated plasma cyclic AMP levels which we have described. These may be merely a reflection of increased corticotrophic or other hormonal activity during and following surgery. It is possible that cyclic AMP and other nucleotides could be released directly from traumatized tissue during operation. However, although our series is small we did not notice any correlation between the degree of trauma and the magnitude of the cyclic AMP peak (Ichikawa et al. in 1971 also failed to correlate the degree of trauma with plasma ACTH peaks). Also, the nucleotides released from damaged tissue would be diluted in the extracellular fluid and subjected to rapid degradation, making it unlikely that any effect on peripheral plasma levels would be observed. A more likely explanation is that cyclic AMP and possibly other adenine compounds escape into the extracellular fluid from all cells as a result of the increased cell membrane permeability which is known to occur during surgery (Flear, 1972). Adenine nucleotides and nucleosides have been previously shown to be capable of crossing cell membranes intact (Axelsson and Holmberg, 1969; Chaudry and Gould, 1970).

However, although we may have demonstrated a true cause and effect relationship between cortisol and cyclic AMP, so many other hormone systems are involved in the response to trauma that one can only hypothesize on our results. Thus, the isolated rat liver will secrete cyclic AMP when perfused with catecholamines (Exton et al., 1972), and this may be of some physiological significance in man. Vetter et al. (1974) have found a significant correlation between plasma levels of cyclic AMP, insulin and glucose during the hours following myocardial infarction. Finally, we do not know the effect of anaesthesia *per se* on plasma cyclic AMP concentrations. Further work is required to elucidate these complex problems.

Acknowledgement

The authors wish to thank Professor I. D. A. Johnston and Mr I. F. McNeil for permission to study their patients and also Mr D. Clark for help in sample collection.

References

ANGELI A., BOCCUZZI G., FRAJRIA R., BISBOCCI D. and CERESA F. (1973) Early variations of plasma cortisol after pulse intravenous injections of dibutyryl cyclic AMP in normal subjects. *Acta Endocrinol.* **72** 753–761.

AXELSSON J. and HOLMBERG B. (1969) The effects of extracellularly applied ATP and related compounds on electrical and mechanical activity of the smooth muscle taenia coli from the guinea pig. *Acta Physiol. Scand.* **75**, 149–156.

BIRKE G., DUNER H., LILJEDAHL S.-O., PERNOW B., PLANTIN L. O. and TROELL L. (1957) Histamine, catecholamines and adrenocortical steroids in burns. *Acta Chir. Scand.* **114**, 87.

BROADUS A. E., KAMINSKY N. I., NORTHCUTT R. C., HARDMAN J. G., SUTHERLAND E. W. and LIDDLE G. W. (1970) Effects of glucagon on adenosine 3′,5′-monophosphate and guanosine 3′,5′-monophosphate in human plasma and urine. *J. Clin. Invest.* **49**, 2237–2245.

BROWN B. L. ALBANO J. D. M., EKINS R. P. and SGHERZI (1971) A simple and sensitive saturation assay method for the measurement of adenosine 3′,5′ cyclic monophosphate. *Biochem J.* **121,** 561–562.

CHAUDRY I. H. and GOULD M. R. (1970) Evidence for the uptake of ATP by rat soleus muscle *in vitro. Biochim. Biophys. Acta* **196**, 320–326.

COOK D. B., GILL G. V., JACKSON I. M. D. and SMART G. A. (1974) Inhibition by dexamethasone of adrenocorticotrophin and cortisol release induced by intravenous infusion of ATP and dibutyryl cyclic AMP in piglets. *J. Endocrinol.* **60**, 65–73.

COOK D. B, GILL G. V. and LATNER A. L. (1975) Submitted for publication.

ESPINER E. A. (1966) Urinary cortisol excretion in stress situations and in patients with Cushing's syndrome. *J. Endocrinol.* **35**, 29–44.

EXTON J. H., LEWIS S. B., HO R. J. and PARK C. R. (1972) The role of cyclic AMP in the control of hepatic glucose production by glucagon and insulin. *Adv. Cyclic Nucleotide Res.* **1**, 91–101.

FLEAR C. T. G. (1972) Electrolyte and body water charges after trauma. *J. Clin. Pathol.* **4**, Suppl. 23, 16–31.

GREEN H. N. and STONER H. B. (1950) *Biological Actions of the Adenine Nucleotides.* London, Lewis.

GREER M. A., ALLEN C. F., GIBBS F. P. and GULLICKSON C. (1970) Pathways at the hypothalamic level through which traumatic stress activates ACTH secretion. *Endocrinol.* **86**, 1404–1409.

HUME D. H., BELL C. C. and BARKER F. (1962) Direct measurement of adrenal secretion during operative trauma and convalescence. *Surgery* **52**, 174–187.

ICHIKAWA Y., KAWAGOE M., NISHIKAE M., YOSHIDA K. and HOMMA M. (1971) Plasma corticotrophin, growth hormone and 11-hydroxy corticosteroid response during surgery. *J. Lab. Clin. Med.* **78**, 882–890.

JOHNSTON I. D. A. (1972) The endocrine response to trauma. *Adv. Clin. Chem.* **15**, 255–285.

KAMINSKY N. I., BROADUS A. E., HARDMAN J. G., JONES D. J., BALL J. H., SUTHERLAND E. W. and LIDDLE G. W. (1970) Effects of parathyroid hormone on plasma and urinary adenosine 3′,5′-monophosphate in man. *J. Clin. Invest.* **49**, 2387–95.

LATNER A. L. and PRUDHOE K. (1973) A simplified competitive protein-binding assay for adenosine 3′,5′-monophosphate in plasma. *Clin. Chim. Acta* **48**, 353–357.

MURPHY B. E. P. (1967) Some studies of the protein-binding of steroids and their application to the routine micro and ultramicro measurement of various steroids in body fluids by competitive protein-binding radioassay. *J. Clin. Endocrinol. Metab.* **27**, 973–990.

ROBISON G. A., BUTCHER R. W. and SUTHERLAND E. W. (1971) *Cyclic AMP.* New York, Academic Press.

STONER H. B. and GREEN H. N. (1950) Studies on the role of the adrenal cortex in adenosine triphosphate shock. *Br. J. Exp. Pathol.* **31**, 603–614.

THOMASSON B. (1959) Studies on the content of 17-OHCS and its diurnal rhythm in the plasma of surgical patients. *Scand. J. Clin. Lab. Invest.* **11**, Suppl. 42.

VETTER N. J., STRANGE R. C., ADAMS W. and OLIVER M. F. (1974) Initial metabolic and hormonal response to myocardial infarction. *Lancet* **1**, 284–288.

WITORSCH R. N. and BRODISH A. (1972) Evidence for acute ACTH release by extrahypothalamic mechanisms. *Endocrinol.* **90**, 1160–1167.

Br. J. Surg. Vol. 62 (1975) 444–447

Early management of corrosive burns of the oesophagus

M. BALASEGARAM*

SUMMARY

One hundred and sixteen patients with early corrosive burns of the oesophagus treated by the author are reviewed. It is emphasized that the all important aspect of management of these patients is prophylactic treatment to avoid stricture of the oesophagus. Early treatment consists of intravenous fluid therapy, broad spectrum antibiotics, sedation, parenteral hydrocortisone and more importantly maintaining the patency of the oesophagus followed by dilatation. The importance of early barium meal studies and oesophagoscopy is stressed.

INGESTION of corrosive liquids is still one of the commonest forms of suicide in Malaysia, especially amongst the lower social class. While a number of instances result in immediate death, most survive to suffer the disabling sequelae of stricture formation of the pharynx, oesophagus or even the stomach. The management of these patients has become a challenging problem.

This article expounds a personal experience in the management of 116 patients with early corrosive burns treated at the General Hospitals of Seremban and Kuala Lumpur, Malaysia, from January 1964 to July 1974. The basis of treatment is the prevention of the development of strictures of the oesophagus following ingestion of the corrosive liquids during the acute phase, thereby reducing the need for surgical replacement.

Materials and methods

The commonest corrosive agent used for attempted suicides was concentrated sodium hydroxide or lye. Other agents included acetic or formic acid and various alkali-containing detergents. Prior to 1964 all patients with early oesophageal burns were admitted and initially treated by the physicians in the medical units. The patients who later developed strictures or stenosis were then referred to the author for further surgical management. Since 1964 almost all the patients with early corrosive burns were admitted directly under the author's care. There were 116 patients in all. Eighty of these patients were females. More than 85 per cent were between the ages of 18 and 30 years. Seventy (60·3 per cent) were of Indian origin, while the rest were Chinese. No Malaysian case was recorded. Marital problems and family disputes including failure to achieve their desired objectives were the commonest reasons for attempting suicide.

Treatment

Early treatment of these patients was aimed at the prevention of strictures or stenosis of the corrosive burns of the pharynx or oesophagus. It consisted of intravenous fluid therapy, broad spectrum antibiotics, sedation and parenteral hydrocortisone in doses of 200 mg every 6 hours. The most important aspect, however, was to maintain the patency of the oesophagus, keeping the lumen of the oesophagus open by means of a Ryle's or Levin's tube passed immediately after admission. Early barium studies and oesophagoscopy were performed to assess the depth and extent of the burns, and appeared to provide an adequate assessment of the extent of injury. Early oesophagoscopy has been shown to be safe, provided that a small instrument is introduced with care and not taken beyond the area of the burns. This regimen was maintained for a period of 3 weeks. The barium studies were repeated on the first and third weeks and subsequently after 3 months or when necessary. All the burns in this series were either deep or intermediate involving the muscularis or the entire depth of the walls of the oesophagus (*Fig.* 1).

After 3 weeks, dilatation therapy was commenced under general anaesthesia in all the patients. More recently, in the light of earlier experience, dilatation has been performed after 10 days. The patients were dilated weekly for 6 weeks, and later monthly for 6 months to a year. They were all seen regularly for up to 3 years, and were advised to see the author immediately if any difficulty in swallowing solids was noted. Sixty-four patients required dilatation for 6 months while the remainder necessitated a year's dilatation.

Results

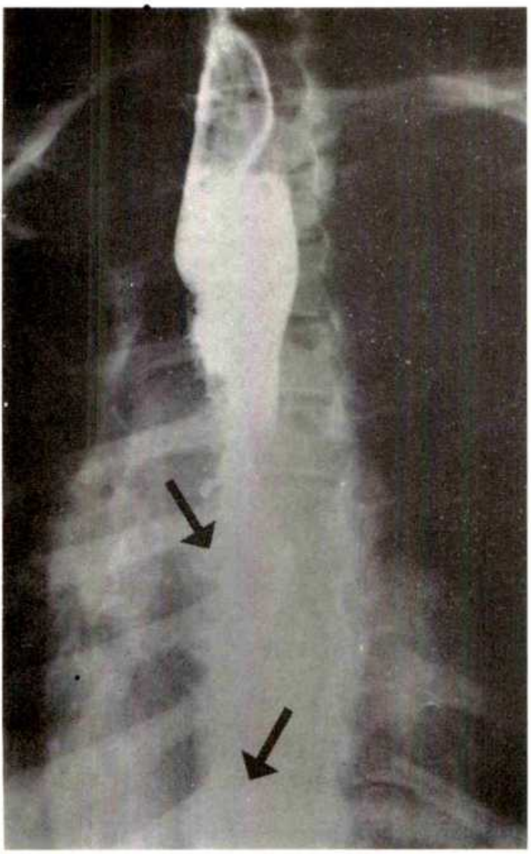
Ten of the 116 patients were admitted in a state of shock, and these all died within a few days of admission in spite of vigorous resuscitation. Autopsy revealed extensive necrosis of the oesophagus and stomach with perforation and mediastinitis.

Of the remaining 106 patients, 8 patients developed strictures of the oesophagus and 3 of the pharynx and larynx. Most of these patients were mentally ill and refused to cooperate with the present treatment regimen. Replacement surgery of the oesophagus and pharynx was performed in these 11 patients using pedicled grafts involving reversed gastric tubes, jejunum or colon.† Three patients developed pyloric stenosis requiring gastro-enterostomy. Three of the 4 patients treated by bouginage developed perforation of the oesophagus. In the fourth the stomach was the site of perforation (*Fig.* 2*a*). Perforation of the oesophagus was treated by intercostal drainage, intravenous fluid

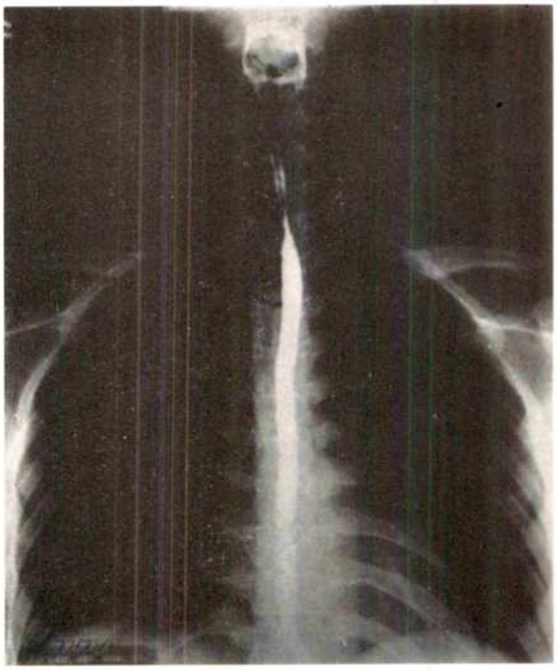
---

* Second Surgical Division, Department of Surgery, General Hospital, Kuala Lumpur, Malaysia.

† Forty-five other patients also had replacement therapy during this period but they were either not treated initially during this period or were referred to the author from other centres. All had established strictures of the pharynx or oesophagus.

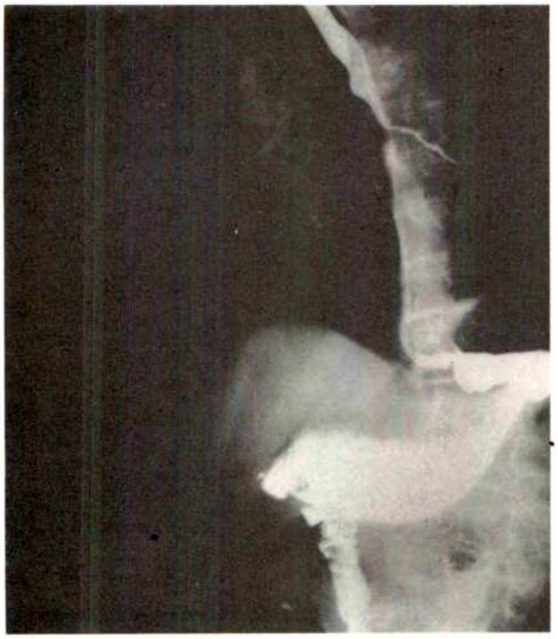


a

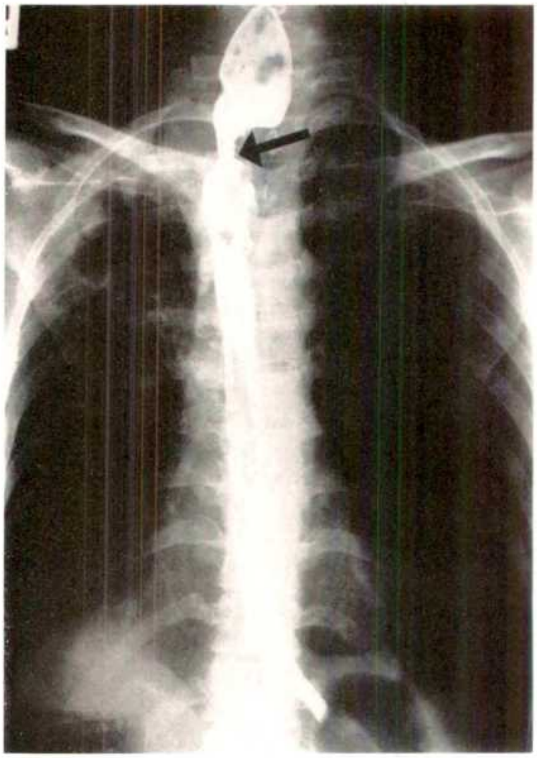


b

Fig. 1. *a*, Barium meal film taken immediately after admission of a patient with corrosive burns. Arrows indicate mediastinitis. Note the fluffy appearance above the top arrow which shows extension of the burn to the full depth of the walls of the oesophagus. *b*, Six weeks after treatment. Note the pipe-stem appearance of the oesophagus.



a



b

Fig. 2. *a*, Barium swallow film showing perforation of the oesophagus following bouginage. *b*, Arrow indicates narrowing due to oesophageal web. This feature can be misdiagnosed as a corrosive stricture.

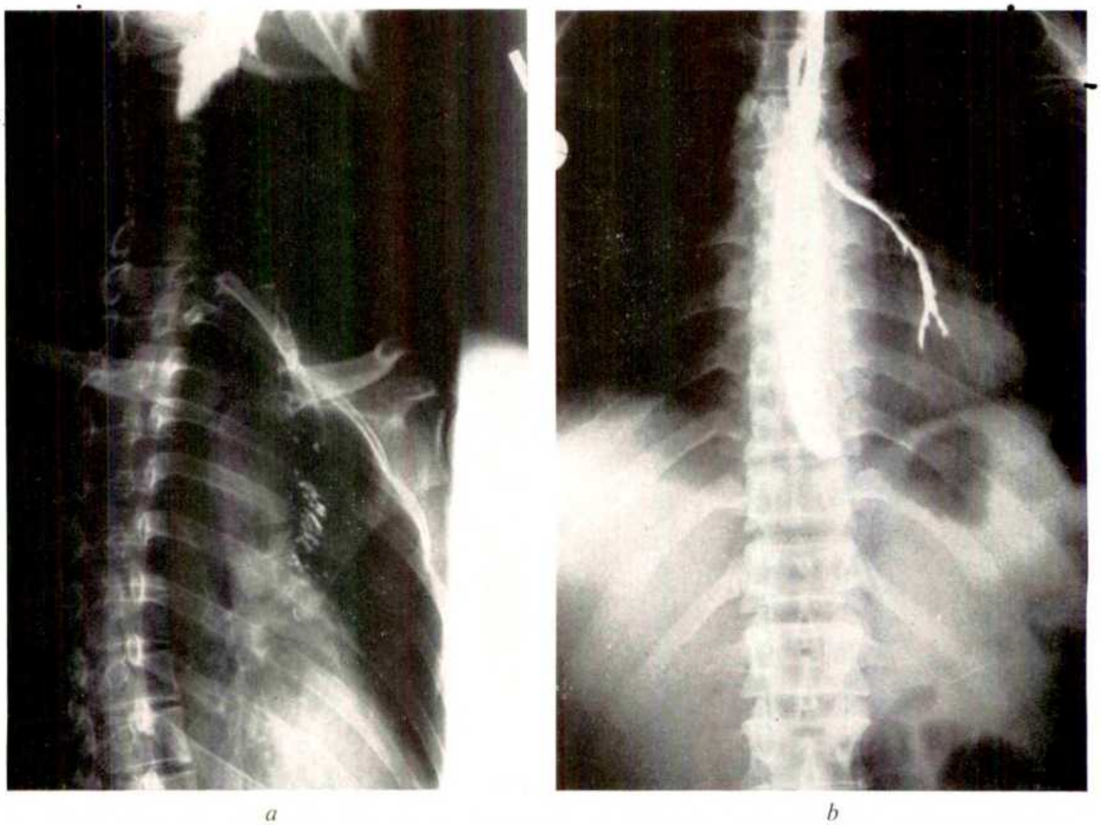


Fig. 3. *a*, Patient with a high stricture requiring surgical intervention. *b*, Patient with a tracheobronchial fistula following ingestion of a corrosive liquid. Such patients require replacement of the oesophagus.

therapy and antibiotics for 3 weeks. These patients recovered fully and were subsequently treated by dilatation. The patient with the perforated stomach refused surgery and died from peritonitis.

Discussion

Corrosive burns of the oesophagus constitute a significant problem in Malaysia because of the common development of severe strictures. Little interest has previously been taken in this persistent problem.

The injury that results from ingestion of corrosive liquids has been well documented (Haller and Bachman, 1964). It is well known that burns in the oral cavity do not necessarily imply extension of the pathology into the oesophagus. Neither is absence of oral burns an indication that there are oesophageal or gastric burns. Clearly the early use of barium studies and oesophagoscopy is of prime importance in first establishing the diagnosis (Knox et al., 1967; Haller, 1971).

It is our view that the classification of oesophageal burns into 'superficial', intermediate' and 'deep' depending on the degree of penetration of the caustic liquid is important. This classification reflects the late changes associated with the healing process which results in subsequent stricture formation. The degree and extent of these changes are proportionate to the length and depth of the acute burns, which in turn are directly related to the amount and concentration of the corrosive liquid consumed and to the duration of its retention in the oesophagus (Storey, 1962). Autopsy reports of patients who died of very extensive burns showed complete destruction and sloughing of the entire lining of the mucosa and muscularis with mediastinitis, and even perforation of the oesophagus and stomach. Many of these patients die within 12–48 hours. In those who survive the damage involved all the layers of the oesophagus, the result being a dense hard fibrotic oesophagus (Cleveland et al., 1963).

Patients with intermediate burns often survive and manifest gangrene of the mucosa due to thrombosis of the submucosal walls with sloughing of the mucosa and submucosa. The sloughing is replaced by granulation tissue which in time is again replaced by fibrous tissue (Burford et al., 1953). In short, the depth of the fibrosis depends upon the severity of the original burn. In all our patients the burns were either deep or intermediate, no doubt because they had swallowed the caustic liquid in large volumes and high concentration with real suicidal intent.

Superficial burns involve only the mucosa, and re-epithelization can be anticipated with little or no evidence of fibrosis or stricture formation. This was confirmed by oesophagoscopy and barium meal studies. In deep burns the appearance of the oesophagus is one of post-inflammatory fibrosis with long strictures and often involvement of the entire circumference of the oesophagus.

The Salzer method of treating corrosive burns introduced in 1920 which consisted of early bouginage was considered unsatisfactory because there was no antibiotic cover at that time to prevent pulmonary or mediastinal infection.

Later, early steroid therapy which was known to prevent inflammatory response was adopted since the major inflammatory reaction occurred during the first 24–48 hours (Viscomi et al., 1961; Webb et al., 1970). This is in keeping with the findings of Palmer (1952), who noted that 80 per cent of all strictures occurred in the first 8 weeks after the burns. However, while the principle of immediate steroid–antibiotic therapy and bouginage appears to be sound, the incidence of oesophageal strictures was still very high indeed. With the advancement of oesophageal surgery, surgeons enthusiastically regarded oesophageal replacement of the oesophagus by stomach, jejunum or large intestine as the best form of treatment (Balasegaram, 1968).

The goal of our present treatment is to forestall late stricture formation by maintaining the patency of the oesophagus and the pharynx by immediate insertion of a Ryle's or Levin's tube on admission, thus keeping the lumen of the pharynx and oesophagus patent, together with commencement of early dilatation. The aim is to salvage an active peristaltic oesophagus into a non-peristaltic pipe-stem tube or a conduit with a lumen of sufficient diameter to enable the patient to swallow, avoiding the hazards of oesophageal surgery. We also believe that these patients are better managed by a surgeon who is particularly interested in this problem, especially as instrumentation and management of complications can be dealt with by him.

However, it must be admitted that in spite of all these measures, replacement surgery was sometimes necessary because of: (*a*) the presence of multiple strictures; (*b*) frequent dilatation; (*c*) failure or refusal of the patient to turn up for regular dilatation; (*d*) high strictures or a fistula between the oesophagus and the trachea or bronchus (*Fig*. 3*a*); (*e*) socio-economic and, more important, psychological reasons. The psychological treatment of these patients is one of the all important factors, considering their state of mind. The very fact that only 12·7 per cent of the patients required replacement surgery with the current form of treatment supports the author's argument.

It is important to note that in this series Indians formed 60·3 per cent of the patients although they comprise only 11 per cent of the population of Malaysia. This is clearly due to the easy availability of corrosive substances in rubber estates where most of them are employed. The Chinese who form 38 per cent of the population had an incidence of only 39·7 per cent. They prefer various forms of drugs or jumping from high buildings and self-immolation. It is the author's opinion that while barbiturates are a kinder form of suicide and popular among the upper class, such attempts are more easily treatable and do not result in agonizing death by comparison with corrosive liquids. Unfortunately, attempted suicide by corrosive liquids does not necessarily end in death and the subsequent suffering of the patient is quite tragic (Balasegaram, 1972).

In conclusion it must be stressed that the all important aspect of management of early corrosive burns is prophylactic treatment to avoid strictures of the oesophagus. A big step forward has therefore been taken and new findings and developments can be expected from the author's present management. However, the real answer to this problem and one that is currently under discussion is Government legislation on the sale and control of corrosive liquids.

Addendum

Since this paper was prepared the author has successfully treated by the present regimen a further 7 cases of suicidal corrosive poisoning due to ingestion of lye.

Acknowledgements

I wish to thank the Director-General of Medical Services, Federation of Malaysia, for permission to publish this paper and to Mrs Jessie Cardoza for typing the manuscript.

References

BALASEGARAM M. (1968) Replacement of hypopharynx and the oesophagus. *Am. J. Surg*. **115**, 279–286.

BALASEGARAM M. (1972) Surgical experiences in Malaysia. *S. Afr. J. Surg*. **10**, 79–87.

BURFORD T. H., WEBB W. R. and ACKERMAN L. (1953) Caustic burns of the oesophagus and their surgical management. A clinico-experimental correlation. *Ann. Surg*. **138**, 453–459.

CLEVELAND W. W., CHANDLER J. R. and LAWSON R. B. (1963) Treatment of caustic burns of the oesophagus, *JAMA* **186**, 262–263.

HALLER J. A. (1971) Management of oesophageal burns. *J. Pediatr*. **6**, 578–584.

HALLER J. A. and BACHMAN K. (1964) The comparative effect of current therapy on experimental caustic burns of the oesophagus. *Pediatrics* **34**, 236–240.

KNOX W. G., SCOTT J. R., ZINTELL H. A., GUTHRIE R. and MCCABE R. E. (1967) Bouginage and steroids used singly or in combination in experimental corrosive oesophagus. *Ann. Surg*. **166**, 930–941.

PALMER E. D. (1952) *Esophagitis due to Corrosive Agents in the Esophagus and its Diseases*. New York, Hoeber, p. 288.

SALZER H. (1920) Early treatment of corrosive esophagitis. *Klin. Wochenschr*. **33**, 307 (quoted by STOREY, 1962).

STOREY C. F. (1962) *Acquired Lesions of the Oesophagus*. Springfield, Ill., Thomas, pp. 109–129.

VISCOMI G. J., BEEKHUIS G. J. and WHITTEN C. G. (1961) Evaluation of early oesophagoscopy and corticosteriod therapy in corrosive injury of oesophagus. *J. Pediatr*. **39**, 356–359.

WEBB W. R., KONTRAS P., ECKER R. R. and SUGG W. L. (1970) An evaluation of steroids and antibiotics in caustic burns of the oesophagus. *Ann. Thorac. Surg*. **9**, 95–98.

Br. J. Surg. Vol. 62 (1975) 448–454

The management of peptic oesophageal stricture

R. C. N. WILLIAMSON*

SUMMARY

Eighty-three adult patients with peptic oesophageal stricture are reviewed with regard to diagnosis and treatment. Sliding hiatus hernia was present in 94 per cent of cases. The strictures were graded according to the degree of stenosis encountered at initial oesophagoscopy, but several other factors influenced the management of each case. Bouginage should always be attempted before proceeding to surgery. Thirty-eight patients were treated by bouginage alone, with 21 (55 per cent) good results and 3 deaths. Forty-five patients came to surgery, with 32 (71 per cent) good results and 3 deaths. Six patients sustained instrumental perforation of the oesophagus with 1 fatality. There was in addition 1 case of silent perforation following self-bouginage, which is believed to be unique. Hiatal herniorrhaphy combined with simple bouginage is recommended where reflux oesophagitis dominates the clinical picture. Local plastic repair (oesophagoplasty) has proved a simple and effective method of treating low annular strictures. Oesophagogastrostomy was carried out in 12 patients without operative loss and with good results in 8 cases; the addition of a pyloroplasty is believed to lessen postoperative reflux.

INJURY to the oesophagus may cause submucosal scarring, leading to permanent stenosis. In this country the commonest injurious agent is gastro-oesophageal reflux, but treatment of the resultant peptic stricture remains controversial. It has been stated that 'bouginage should be the method of choice in every case unless one is dealing with severe haemorrhage or perforation' (Benedict, 1966). Most British surgeons, however, advocate operation for the majority of cases (Editorial, 1968), though this may vary from local plastic repair to extensive resection with oesophageal replacement. The present communication reviews a large series of patients with peptic oesophageal stricture, with particular regard to their diagnosis and treatment in a district thoracic surgical unit.

Patients

The series comprises 83 patients with peptic stricture treated at Peppard Hospital, Oxfordshire, during the 10-year period 1962–71 under the care of one consultant thoracic surgeon. *Table I* shows that this was by far the commonest aetiological type of benign oesophageal stricture seen during this period. All the patients were followed up for a minimum of 2 years after treatment. The total includes 49 women and 34 men, aged from 14 to 89 years with a mean of 68·2 years. The maximal incidence occurred during the seventh and eighth decades, two-thirds of patients being over the age of 70. Not surprisingly this elderly population had a high incidence of cardiorespiratory disease, 11 patients being severely incapacitated.

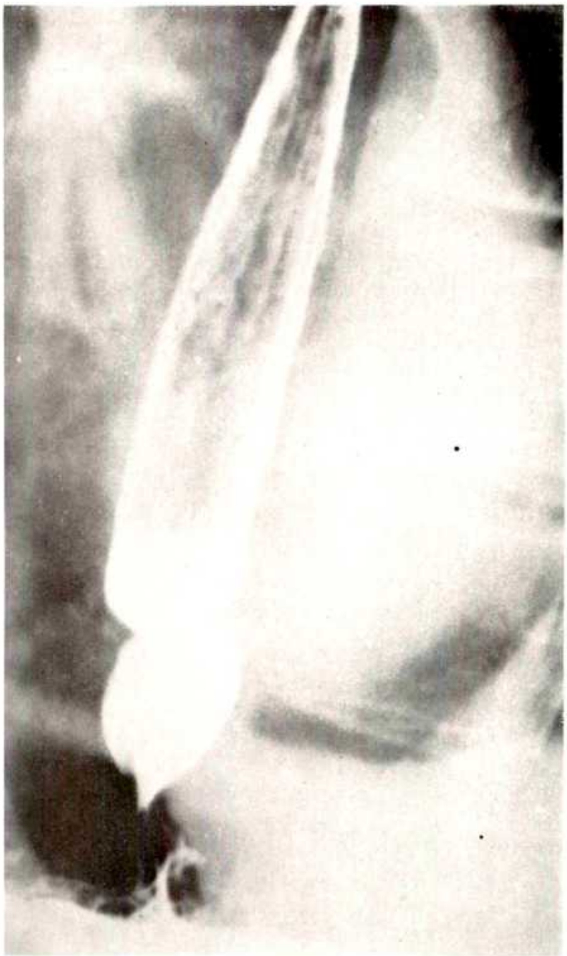


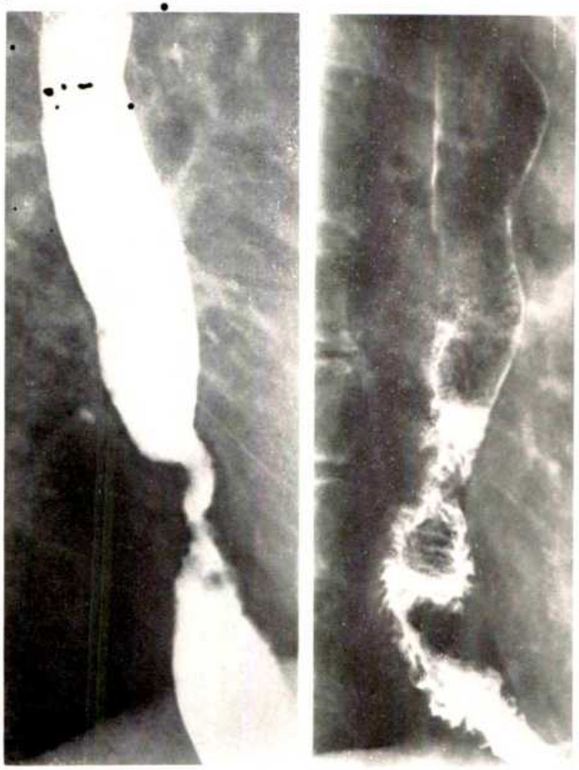
Fig. 1. Barium swallow film showing an early annular stricture of the lower oesophagus. This caused surprisingly severe symptoms but was successfully treated by local plastic repair (oesophagoplasty).

Table I: AETIOLOGICAL TYPES OF BENIGN OESOPHAGEAL STRICTURE

Aetiological type:	No. of cases:
Peptic	83
Anastomotic	8
Sideropenic	2
Pemphigoid	1
Irradiation	1
Corrosive	1
Total	96

---

* Royal Berkshire Hospital, Reading.
Present address: United Bristol Hospitals.



a *b*

Fig. 2. *a*, 'Ascending oesophageal fibrosis'. Barium swallow film showing an elongated peptic stricture. *b*, The appearance on a barium swallow film following resection of the stricture with jejunal replacement. The patient obtained an excellent result.

Sliding hiatus hernia was demonstrated in 78 of the 83 cases (94 per cent), while the remaining 5 patients all had clinical and endoscopic features of reflux oesophagitis. Three patients with no antecedent gastro-oesophageal symptoms developed an acute postoperative stricture, in each case following colonic surgery.

Diagnosis

Clinical

Table II shows that dysphagia was the only constant symptom. It varied greatly in severity and duration and 7 patients presented with complete oesophageal obstruction (aphagia). It is notable that one-third of the patients had no previous history of reflux oesophagitis.

Radiological

Apart from 2 patients with aphagia who underwent emergency oesophagoscopy, all the strictures were first demonstrated by barium swallow examination. *Figs.* 1 and 2 illustrate the two classic types, namely annular stricture caused by a localized ring of fibrous tissue, and ascending oesophageal fibrosis (Kelly, 1936) where scarring extends for several centimetres with muscular hypertrophy, peri-oesophagitis and mediastinal adenopathy. In 12 strictures subsequently shown to be benign there was radiological suspicion of carcinoma; 5 of these also appeared irregular at endoscopy so that the possibility of carcinoma became a major factor in advising surgery. *Fig.* 3 demonstrates another pitfall in radiological diagnosis.

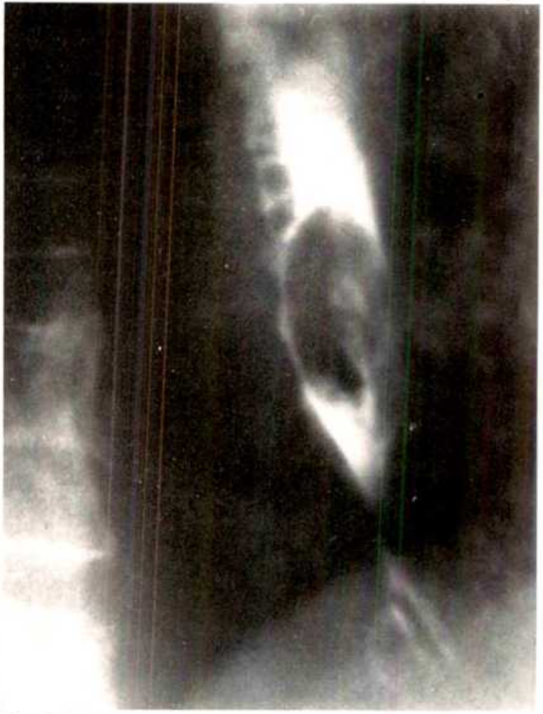


Fig. 3. Barium swallow film magnified to show a rounded filling defect in the lower oesophagus. This was reported as a leiomyoma but at thoracotomy the 'tumour' proved to be a peanut, swollen and impacted above an annular stricture. Oesophagoplasty was successfully performed.

Table II: SYMPTOMS OF PEPTIC STRICTURE

Symptom	No. of cases	%
Dysphagia	83	100
Reflux oesophagitis (heartburn, acid brash etc.)	55	66
Regurgitation of solids	42	51
Weight loss (>6·3 kg)	19	23
Haematemesis	8	9
Inhalation pneumonitis	5	6
Hiccup	5	6

Endoscopic

In nearly every case the presence of a stricture was confirmed at oesophagoscopy and definitive treatment by bouginage was attempted at the same time. Some degree of oesophagitis was observed in 45 patients (54 per cent). *Fig.* 4 shows that the large majority of peptic strictures were confined to the lower third of the oesophagus, as expected. The strictures were graded according to the degree of stenosis encountered at the initial oesophagoscopy as follows:

Grade I: Slight stenosis easily negotiated.
Grade II: Moderate stricture dilated without difficulty.
Grade III: Tight stricture only dilated with difficulty.
Grade IV: Impassable stricture.

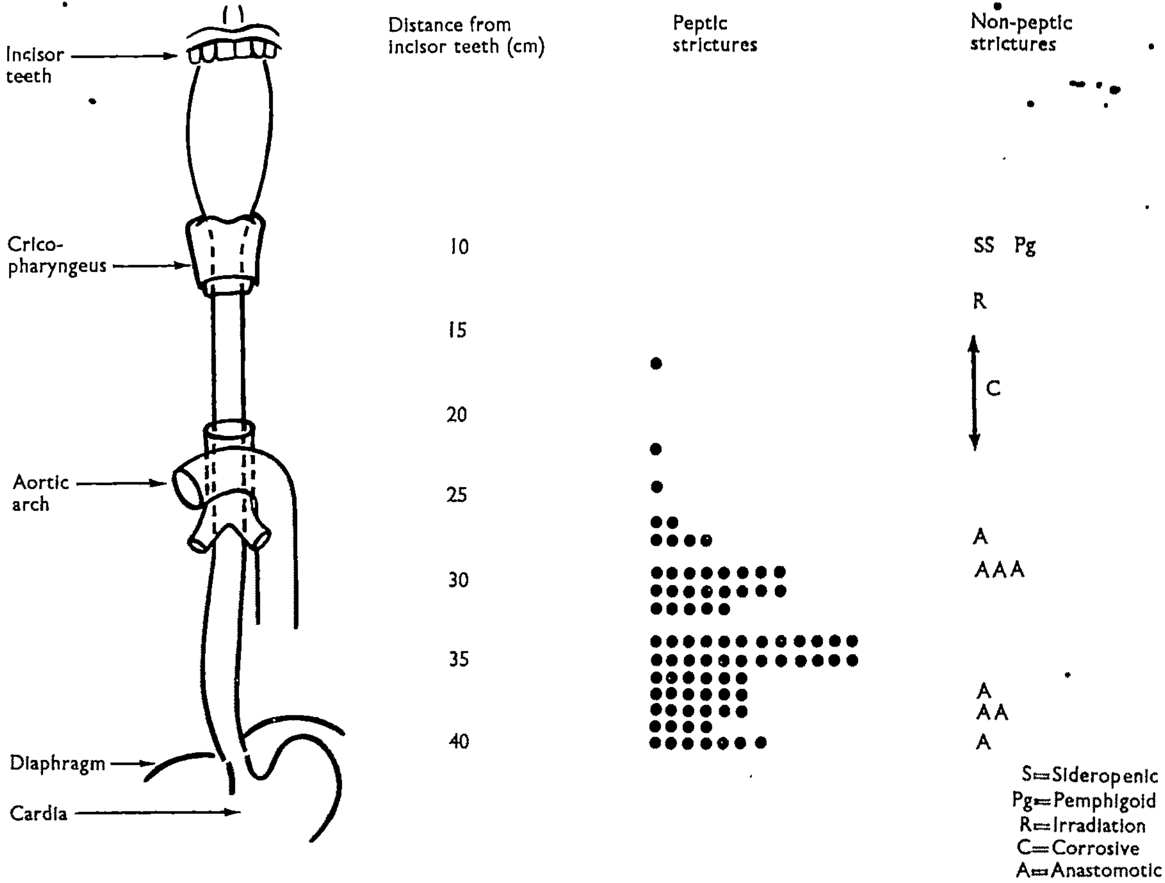


Fig. 4. Diagram to show the level of benign oesophageal strictures at endoscopy. Each peptic stricture is marked by a black circle. Strictures of non-peptic origin are included for comparison. The highest peptic stricture was found at 18 cm from the incisor teeth; it proved amenable to bouginage.

Histological

In 53 patients carcinoma was excluded as far as possible by the examination of biopsy or operative specimens, and in another 13 patients the oesophagus was directly inspected at thoracotomy. In the remaining 17 cases the diagnosis rested upon the continued absence of suspicious clinical, radiological or endoscopic features at follow-up. There was no incidence of a benign peptic stricture undergoing malignant change.

Methods of treatment

The primary objective of treatment was to enable every patient to swallow sufficiently well to maintain his weight and nutritional status, albeit with some modification of diet. Associated oesophagitis was treated by a standard medical régime (Bennett, 1973). Dilatation of strictures was carried out using Neoplex or metal Souttar bougies, usually under general anaesthesia and always under direct endoscopic control, though 11 patients whose stricture demanded repeated dilatation at frequent intervals were taught to pass their own bougies under a local anaesthetic. Fibre-optic oesophagoscopy was not available during the period of this study. The following surgical methods were employed.

Repair of hiatus hernia entailed exposure of the oesophagus within the chest, usually via a left thoracolaparotomy. Reduction of the hernia was achieved as far as possible and the hiatus was repaired by anterior apposition of the crura; routine Heineke–Mikulicz pyloroplasty was carried out additionally.

Operative dilatation of awkward low strictures was performed via a gastrotomy to allow digital dilatation or the retrograde passage of bougies. In a few such cases a Celestin tube was passed from above, right through the stricture and out, to ensure that adequate dilatation had been achieved. In certain selected cases the tube was left *in situ*.

Oesophagoplasty or local plastic repair was reserved for low annular strictures which were exposed within the chest, incised longitudinally through all coats and closed transversely with one layer of interrupted catgut sutures, in a manner akin to Heineke pyloroplasty.

Resection of the stricture was generally performed through a left thoracolaparotomy with direct oesophagogastric anastomosis and the addition of a pyloroplasty. Oblique transection of the stomach allowed the creation of a gastric tube for anastomosis with the transected oesophagus. In 3 cases a segment of jejunum or right colon was brought up to bridge the defect following an extensive resection.

The long term result of treatment in each case was assessed as follows:

Good: Manages virtually normal diet; minimal dysphagia.

Moderate: Careful diet needed; occasional regurgitation of food.

Poor: Liquid diet; frequent dysphagia and regurgitation.

Results of treatment

Of 55 patients presenting with symptoms of reflux, 24 continued to require medical treatment for this after either bouginage or surgery. However, only 3 patients in all had symptoms of reflux aggravated by local treatment of the stricture.

Table III shows that whatever the grading of the stricture at initial endoscopy roughly equal numbers of patients were treated by surgery and bouginage. Though grade I strictures responded readily to simple bouginage, surgery was often required in this group for severe associated reflux oesophagitis. The largest group of strictures belonged to grade II; of these, half were treated surgically and half by bouginage, which usually became progressively easier. Grade III and IV strictures were very unpredictable. Five patients reported some improvement in swallowing despite unsuccessful bouginage, 2 of them requiring no further treatment. Five strictures, initially impassable, subsequently yielded to bouginage, and the long term result in these difficult cases was sometimes surprisingly good. Nonetheless difficulties encountered during bouginage (including previous endoscopic perforation in 3 cases) were a common indication for surgery (*Table IV*) if dysphagia subsequently recurred.

The results of treatment are shown in *Table V*. Thirty-eight patients (46 per cent) were managed by bouginage alone, 17 requiring only one dilatation carried out at the time of diagnostic oesophagoscopy. Where the result remained only 'moderate' after repeated bouginage surgery was advised unless contraindicated by extreme age or infirmity, and these patients comprise the 'bouginage ineffective' group listed in *Table IV*. Forty-five patients were treated surgically (54 per cent) and all but 5 of these had undergone a previous trial of bouginage. Three types of surgical procedure were performed:

1. *Repair of hiatus hernia*

A relatively young group of patients with marked oesophagitis was submitted to anti-reflux surgery with bouginage of the associated grade I or II stricture. This combination was employed in 1 case of grade III stricture presenting in a girl of 14, but the result was poor and she required subsequent resection with oesophagogastrostomy. *Table V* shows that the results of this combined procedure were otherwise very

Table III: GRADING OF PEPTIC STRICTURES

Grade	No. of cases	Treatment	
		Bouginage	Surgery
I	11	5	6
II	44	22	22
III	9	4	5
IV	11	6	5
Unclassified*	8	1	7
Total	83	38	45

* Stricture not seen at endoscopy or bouginage not attempted.

Table IV: INDICATIONS FOR SURGERY

Indication:	No. of cases:
Bouginage difficult	14
Bouginage ineffective	13
Reflux oesophagitis	12
Carcinoma suspected	5
'Leiomyoma' (*Fig.* 3)	1
	Total 45

Table V: RESULTS OF TREATMENT

Procedure	No. of cases	Result			
		Good	Moderate	Poor	Death
Bouginage	38	21	14	0	3
Surgery*	45	32	9	1	3
Repair of hiatus hernia	12	10	1	1	0
Retrograde dilatation	6	5	0	1	0
Oesophageal intubation	9	3	4	0	2
Oesophagoplasty	7	6	1	0	0
Oesophagogastrostomy	12	8	3	1	0
Jejunum/colon replacement	3	2	0	0	1
Total	83	53 (64%)	23 (28%)	1 (1%)	6 (7%)

* In 4 cases more than one type of operative procedure was carried out and the final surgical result is recorded.

Table VI: CASES OF INSTRUMENTAL PERFORATION OF THE OESOPHAGUS

Age	Sex	Difficulty at endoscopy	Delay in onset of symptoms (h)	Level of perforation	Treatment	Complications
70	F	Postcricoid	24	Cervical	Conservative	Nil
77	F	Postcricoid	24	Cervical	Conservative	Nil
88	F	Nil	24	Thoracic	Conservative	Empyema thoracis
37	F	Nil	24	Thoracic	Conservative	Peri-oesophageal abscess
78	F	Grade III stricture	4	Thoracic	Operative	Nil
79	F	Grade III stricture	2	Thoracic	Operative	Death

satisfactory within the period of follow-up, even though extensive peri-oesophagitis often prevented complete reduction of the hernia. The stricture was treated by prior endoscopic bouginage or, in 2 cases, by retrograde digital dilatation at the time of operation. In 3 cases bouginage was required for a short time postoperatively as well.

2. *Limited surgery to the stricture*

Operative dilatation was performed in 6 cases, including 1 man who underwent retrograde bouginage no less than three times in 4 months before obtaining a satisfactory and lasting result. The 1 patient with a 'poor' result had sustained a previous endoscopic perforation and was deemed too frail for any further procedure.

Oesophageal intubation was reserved for a group of very elderly and unfit patients in whom bouginage was inadequate but major surgery impossible. It was not a particularly satisfactory procedure, for 2 patients died and several of the survivors had trouble with the tube. In 3 cases it slipped up the oesophagus to cause renewed dysphagia and require removal. One old lady passed her tube in two pieces per rectum to the consternation of the nursing staff.

Oesophagoplasty was carried out in 7 cases of localized annular stricture close to the cardia (*Figs.* 1, 3). The results were good apart from 1 patient with residual dysphagia due to disordered oesophageal motility. Two patients with anastomotic stricture were treated with equal success by this procedure.

3. *Resection*

Oesophagogastrostomy was carried out in 12 cases; the oldest patient was 72 and all enjoyed reasonable general health. Although several had initial postoperative problems 8 patients obtained a 'good' result. Reflux oesophagitis spoilt the result in 3 cases, aggravated in one by obesity and in another by aspirin. Four patients needed limited postoperative bouginage. The only 'poor' result was in a patient who bled from an anastomotic ulcer, requiring further resection with jejunal interposition. This operation was performed in one other patient (*Fig.* 2) and neither case of jejunal replacement has required any further treatment. The sole case of colonic interposition died following an anastomotic leak on the tenth day, this being the only fatality among the 14 cases of resection.

Complications

Three patients died following endoscopic bouginage, a mortality of 7·9 per cent. The causes of death were pulmonary embolism, chronic chest infection and instrumental perforation. Two patients sustained a limited gastro-intestinal haemorrhage following instrumentation.

There were 6 cases of instrumental perforation of the oesophagus during 270 endoscopies performed for benign stricture, an incidence of 2·2 per cent; the details are shown in *Table VI*. Strangely, 5 of the 6 patients had undergone previous uneventful bouginage. In 2 cases dilatation was completed without suspicion of trauma, in 2 difficulty was encountered at the postcricoid level and in 2 the stricture itself was difficult to dilate. These last 2 both presented within a few hours of the accident and were treated surgically, though in 1 case operation was delayed for 48 hours and the patient died. The other 4 were treated conservatively with intravenous fluids and antibiotics in elixir form. Two of these developed a local abscess but made a complete recovery following drainage; the 2 patients with postcricoid perforation had minimal upset.

The following case report illustrates one remarkable complication of self-bouginage:

> A 65-year-old man presented with dysphagia, epigastric pain and regurgitation of solids. Gross kyphosis was noted. Barium swallow examination showed a large hiatus hernia and an irregular stricture at the cardia with rigid margins suspicious of carcinoma. Endoscopy revealed an inflamed fibrous stricture at 35 cm which could not be dilated; biopsies showed no carcinoma. Ten days later the stricture was successfully dilated. The patient survived a major pulmonary embolus thereafter and his swallowing was much improved. In the following year the stricture was dilated three times and as it remained tight he was taught self-bouginage; this he practised on three occasions, the last time passing a no. 43 FG Neoplex bougie without difficulty. After this he began to develop abdominal pain and was readmitted with a small haematemesis 16 days after self-bouginage. Findings of peritonitis led to laparotomy and the discovery of a large left subhepatic abscess with a second smaller abscess within the liver. These were drained and the patient made an uneventful recovery. Two subsequent attempts at endoscopic bouginage have failed but his swallowing is reasonably satisfactory.

Postoperatively, 3 patients died, a mortality of 6·7 per cent. Two deaths (from haematemesis and aspiration pneumonia respectively) followed insertion of a Celestin tube. The other fatality followed rupture of an interposed segment of colon. There was 1 case of postoperative chylothorax requiring thoracic duct ligation and one of strangulated diaphragmatic incisional hernia.

Discussion

Reflux oesophagitis, the commonest disease affecting the gullet, may eventually lead to peptic stricture in 2–3 per cent of cases (Johnson and Lukash, 1970). Under certain circumstances (Allison, 1970), and especially after any major abdominal operation (Benedict and Gillespie, 1954), this process may develop rapidly; in the present series 3 patients developed an acute peptic stricture, in each case following colonic surgery.

Benedict (1966) advocated bouginage for nearly every peptic stricture, reporting good results in 70 per cent of 133 patients. Many of these with unrepaired hiatal hernia became entirely symptom-free following bouginage. Barrett (1962) objected to simple bouginage on the grounds that it broke down a natural barrier against the upwards spread of oesophagitis, but in the present series reflux was only aggravated in 3 patients undergoing either bouginage or limited surgery to the stricture. Nevertheless, few surgeons would agree with Benedict that haemorrhage and perforation comprise the only indications for surgery. Only 55 per cent of our patients obtained a good result from bouginage alone, and its failure to procure lasting relief from dysphagia was a common indication for operation. Likewise, difficulty encountered during previous bouginage and the possibility of carcinoma will usually demand surgical intervention.

There were 6 cases of instrumental perforation during endoscopy, an incidence of 2·2 per cent, with 1 fatality. Raptis and Milne (1972) reported 4 such cases in their series of 100 benign strictures, again with 1 fatality. The overall incidence of perforation during all upper gastro-intestinal endoscopies is 0·5–0·7 per cent (Elner and Dahlback, 1962; Mark and Knauer, 1969), occurring most frequently in the cervical oesophagus in elderly women (Wychulis et al., 1969). This accident, of which 2 examples are reported here, can usually be managed conservatively (Hardin et al., 1967). Dilatation for benign or malignant stricture is the second commonest cause of iatrogenic perforation (Loop and Groves, 1970). The evidence suggests that patients who present with features of ruptured thoracic oesophagus within a few hours of endoscopy require immediate surgical exploration. The case of silent perforation during self-bouginage is believed to be without precedent, although Goldstein and Sherlock (1966) reported 1 case of unsuspected perforation following endoscopic bouginage carried out under a local anaesthetic.

Endoscopic bouginage is therefore not without risk and in the present series carried a mortality (7·9 per cent) akin to that of operation (6·7 per cent). Furthermore, the 3 postoperative deaths occurred in patients in whom surgery had been necessitated by failure of bouginage. Taken in isolation, the tightness of the stricture was found to be a poor guide in determining the need for surgery. The natural history of peptic stricture appears to be unpredictable and the degree of reflux oesophagitis varies widely between cases. Age and infirmity often preclude the adoption of more vigorous methods of treatment, though it may be a matter of judgement whether multiple bouginage or limited surgery carries a greater risk in such cases. Twenty-one per cent of all cases required no other treatment than a single dilatation of the stricture carried out at the time of diagnostic oesophagoscopy. The policy was therefore to attempt bouginage in nearly every case, but if this should fail, to proceed to surgery, the choice of operation depending upon the degree of oesophagitis and the extent of the stricture.

Where symptoms of reflux overshadow those of stricture lasting relief from dysphagia can usually be achieved by combining hiatal repair with simple bouginage (Hill et al., 1970). Palmer (1968) reported 7 patients treated in this way who subsequently required bouginage as often as those whose hernia had been left unrepaired, but in the present series this was not the case: of 11 patients with early or moderate grades of stricture submitted to hiatal herniorrhaphy, only 3 needed any postoperative bouginage at all and that only for a brief period. This was in spite of the fact that gross peri-oesophagitis often prevented complete reduction of the hernia.

Where the stricture itself is the dominant feature the choice lies between limited surgery and resection. Retrograde dilatation may be of temporary value in the management of an awkward low stricture, especially if there are additional reasons for laparotomy. Intubation is probably best reserved for malignant strictures. Tubes tend to work loose from benign strictures after a time and reflux can be difficult to control (Holden and Wooler, 1971). Oesophagoplasty is a simple and effective method of relieving annular strictures in the lower oesophagus and avoids the need for resection in these cases. Good results were obtained in 6 out of 7 patients and postoperative reflux did not constitute a serious problem.

The troublesome minority of long strictures ('ascending oesophageal fibrosis') will usually demand resection and some kind of oesophageal replacement. Allison (1970) has stated that direct oesophagogastric anastomosis merely reproduces the lesion that caused the original stricture, while Skinner and Belsey (1967) reported a mortality of 14·5 per cent in 106 patients so treated. Twelve cases of oesophagogastrostomy are presented here without operative loss, though 3 of these needed postoperative medical treatment for reflux. Pyloroplasty was routinely performed. Raptis and Milne (1972) omitted this step in 41 oesophagogastrostomies performed for benign stricture and encountered anastomotic strictures in 10 of these. Eight of the 10 were found to have pyloric obstruction and were relieved by a subsequent pyloroplasty.

Interposition of jejunum or colon must add to the morbidity and mortality of resection though it avoids the chance of any future reflux of acid peptic juice. Allison reported excellent results in 50 patients thus treated, with a mortality of only 4 per cent; jejunum was found to be more active than colon in conveying food.

Acknowledgements

I am indebted to Mr Clement Grimshaw for allowing me to study the patients under his care at Peppard Hospital. I am also grateful to Professor M. H. Irving and Mr A. G. Cox for their help and encouragement in completing this paper. The illustrations were kindly provided by Mr Lionel Williams, Medical Photographer at the Royal Berkshire Hospital, Reading.

References

ALLISON P. R. (1970) Peptic oesophagitis and oesophageal stricture. *Lancet* **2**, 199–201.

BARRETT N. R. (1962) Benign stricture in the lower oesophagus. *J. Thorac. Cardiovasc. Surg.* **43**, 703–715.

BENEDICT E. B. (1966) Peptic stenosis of the esophagus: a study of 233 patients treated with bouginage, surgery or both. *Am. J. Dig. Dis.* **11**, 761–770.

BENEDICT E. B. and GILLESPIE J. E. O'N. (1954) Peptic stenosis of the esophagus. *Surg. Gynecol. Obstet.* **98**, 494–502.

BENNETT J. R. (1973) Symposium on gastro-oesophageal reflux: the physician's problem. *Gut* **14**, 246–249.

EDITORIAL (1968) The vulnerable oesophagus. *Lancet* **2**, 267–268.

ELNER A. and DAHLBACK O. (1962) Instrumental perforation of the esophagus. *Acta Otolaryngol.* (*Stockk.*) **54**, 279–286.

GOLDSTEIN M. J. and SHERLOCK P. (1966) Silent esophageal perforation following esophagoscopy. *Gastrointest. Endosc.* **13**, 22–25.

HARDIN W. J., HARDY J. D. and CONN J. H. (1967) Esophageal perforations. *Surg. Gynecol. Obstet.* **124**, 325–331.

HILL L. D., GELFAND M. and BAUERMEISTER D. (1970) Simplified management of reflux oesophagitis with stricture. *Ann. Surg.* **172**, 638–651.

HOLDEN M. P. and WOOLER G. H. (1971) Mousseau–Barbin tubes for benign strictures of the oesophagus. *Thorax* **26**, 619–622.

JOHNSON R. B. and LUKASH W. M. (1970) Dilatation of esophageal strictures. *Mod. Treat.* **7**, 1190–1203.

KELLY A. B. (1936) Some oesophageal affections in young children. *J. Laryngol. Otol.* **51**, 78–99.

LOOP F. D. and GROVES L. K. (1970) Esophageal perforations. *Ann. Thorac. Surg.* **10**, 571–587.

MARK J. B. D. and KNAUER C. M. (1969) Use of the onlay gastric patch in instrumental rupture of the esophagus. *J. Thorac. Cardiovasc. Surg.* **57**, 883–886.

PALMER E. D. (1968) The hiatus hernia–esophagitis–esophageal stricture complex. Twenty-year prospective study. *Am. J. Med.* **44**, 566–579.

RAPTIS S. and MILNE D. M. (1972) A review of the management of 100 cases of benign stricture of the oesophagus. *Thorax* **27**, 599–603.

SKINNER D. B. and BELSEY R. H. R. (1967) Surgical management of esophageal reflux and hiatus hernia. Long term results with 1030 patients. *J. Thorac. Cardiovasc. Surg.* **53**, 33–54.

WYCHULIS A. R., FONTANA R. S. and PAYNE W. S. (1969) Instrumental perforations of the esophagus. *Dis. Chest* **55**, 184–189.

Br. J. Surg. Vol. 62 (1975) 455–461

The effect of raising the concentration of potassium in the blood or intestinal lumen on the transport of potassium in the dog intestine

ANNE HARDY-SMITH AND R. SHIELDS*

SUMMARY

The rates of transport of potassium, sodium and water across the intestinal mucosa of Thiry-Vella fistulas of colon and ileum, were studied in dogs in two experimental situations; (1) following intravenous infusion of potassium (15 mEq) over 30 minutes and (2) during variations in the intraluminal concentration of potassium in the range 0·8–16·0 mEq/l.

Following intravenous infusion of potassium the rates of potassium secretion into the colon were usually increased; the rates of sodium and water absorption were either unchanged or decreased. The unidirectional rate of movement of potassium into the lumen increased as the concentration difference across the mucosa increased; the movement of potassium in the opposite direction remained relatively constant. The unidirectional movement of sodium and water into the lumen of the colon also increased but to a lesser extent. The effect on potassium transport in the ileum was not so marked.

With increase in the intraluminal concentration of potassium there was a decrease in the rate of net potassium secretion in both colon and ileum. The rates of net absorption of sodium and water were not significantly altered. Unidirectional potassium movement into the body increased in all the ileal fistulas.

THE intestinal absorption of electrolytes can be influenced by changes in the composition of the body (Shields, 1964; Fordtran and Dietschy, 1966; Vogel et al., 1969; Sladen, 1972). In sodium depletion there is an increased intestinal absorption of sodium and an increased secretion of potassium (Clarke et al., 1967). Similar changes are produced by aldosterone (Edmonds, 1969), whose secretion is known to be increased during sodium depletion (Leutscher and Curtis, 1955; Ross, 1962; Wright, 1962). The secretion of aldosterone is also stimulated by loading the body with potassium (Falbriard et al., 1955; Laragh and Stoerk, 1955; Leutscher and Curtis, 1955; Gann et al., 1964).

However, the effect of potassium overloading on the intestinal absorption of electrolytes is not known. Such knowledge has obvious clinical relevance. Thus, when potassium is being infused intravenously the dose and rate of administration have to be carefully controlled, whereas there appears to be no such restriction when potassium is being given by mouth (Black, 1953). The greater safety of oral potassium may be due to reduced intestinal absorption in addition to its rapid renal excretion as the concentration of potassium in the blood increases.

To study intestinal absorption during potassium loading we used dogs with Thiry-Vella fistulas. As the dogs would not readily eat a diet containing quantities of potassium sufficiently large to raise the body potassium, attempts to produce prolonged accumulation of potassium were generally unsuccessful. However, intravenous infusion of potassium with or without previous dietary administration of potassium resulted in a considerable transient increase in the plasma potassium concentration. This enabled us to study the effects of increasing the blood potassium concentration on the intestinal transport of electrolytes. In addition, the effect of increasing the concentration of potassium in the lumen was studied for comparison.

Materials and methods

Thiry-Vella fistulas of ileum (12–27 cm) or colon (10–13 cm) were prepared in 4 beagles; 2 dogs had a colonic fistula and 2 had an ileal fistula. Three of these dogs were replaced after 18 months; the body weights ranged from 9 to 19 kg.

The dogs were studied over a period of several months under three conditions; control, following rapid intravenous infusion of potassium and during intraluminal potassium administration:

a. Under control conditions the dogs received an infusion of 30 ml aqueous glucose solution (5 per cent w/v) via a cephalic vein at a rate of 1 ml/min immediately before the absorption tests.

b. Following rapid intravenous infusion of potassium. Instead of the glucose solution, 30 ml 0·5 N-KCl (i.e. 15 mEq potassium) were infused at a rate of 1 ml/min. In some experiments the dogs had received a dietary supplement of 240 mEq potassium and 120 mEq sodium per day for either 14 or 28 days before intravenous infusion.

c. Intraluminal administration was carried out in the absence of any intravenous infusion by adding potassium chloride to the basic intestinal test solution to give concentrations of 0·8, 4·0, 11·0 and 16·0 mEq/l of potassium.

Absorption tests, each lasting 10 minutes, were carried out over a period of 5–7 hours using a method similar to that described by Shields et al. (1966). During the period of raised plasma potassium concentration the interval between tests was reduced to 15 minutes to allow more tests to be performed.

After an initial period of rinsing the fistula with modified Tyrode's solution (Code and McIntire,

---

* Department of Surgery, University of Liverpool.

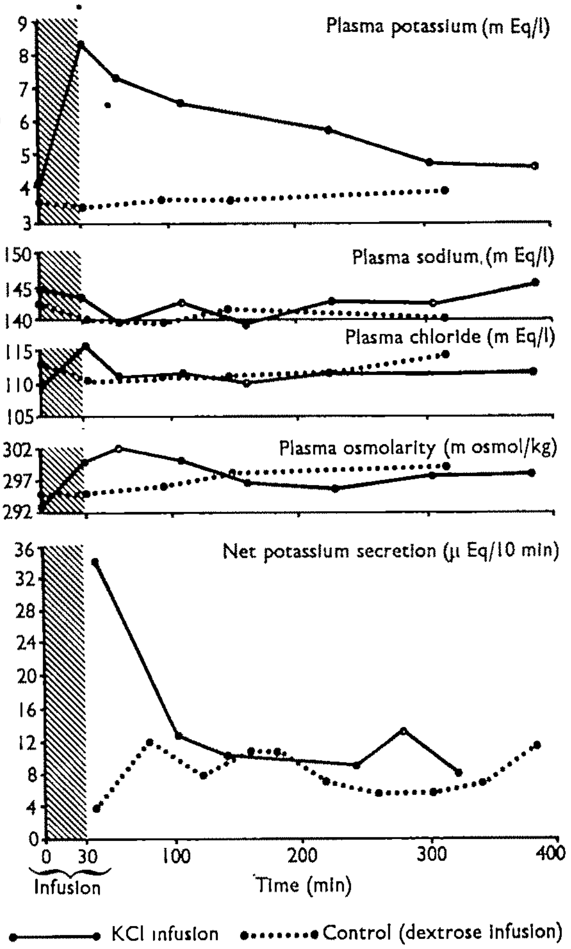


Fig. 1. Changes in the plasma concentration of electrolytes and the net secretion of potassium by the colon in one dog following intravenous infusion of potassium chloride (15 mEq in 30 minutes).

1956) a known volume (20 or 25 ml, depending on the size of the fistula) of the modified test Tyrode's solution containing the radioactive isotopes ^{24}Na and ^{42}K, and the stable isotope deuterium oxide (D_2O, 1 per cent w/v) was installed into the Thiry-Vella fistula. After 10 minutes, as much as possible of the luminal solution was withdrawn and the volume of aspirate measured. Residual test solution in the fistula was measured by rinsing with Tyrode's solution.

Radioactive sodium and potassium in both the rinse and the aspirate were determined by differential counting using a Nuclear-Chicago γ-counter. The volume of residual test solution was calculated from the amount of radioactivity acquired by the rinse. Blood samples were collected before infusion and at intervals after infusion.

Concentrations of sodium and potassium in plasma and aspirate were measured by flame photometry. Concentrations of deuterium oxide in the aspirate were determined by infrared spectrophotometry using the following modification of the method described by Berglund-Larsson (1956). The measurements were carried out in a Perkin-Elmer infrared spectrophotometer, Model no. 177, using universal demountable cells with 0·075 polymeric spacers between quartz windows. A calibration curve was prepared by plotting optical density at 2510 cm^{-1} against atom per cent D_2O over the range 0–1·2 per cent.

The plasma concentration of chloride and the osmolarity were determined using a chloride meter and a freezing point depression osmometer respectively. Packed cell volumes were measured using a microhaematocrit centrifuge.

The concentrations of electrolytes in the red blood cells were measured in the blood samples taken before infusion and in the final sample. The samples were diluted 1 : 1 with standard electrolyte solution (140 mEq/l sodium and 6 mEq/l postassium), frozen overnight, thawed while shaking on a Luckham's Rotatest and then centrifuged at 3500 rev/min. Electrolyte concentrations were measured by flame photometry and the red cell concentrations calculated using the method of Blackmore et al. (1963).

Whenever possible, urine electrolytes were measured by flame photometry in two consecutive 24-hour specimens after the absorption tests. Some of these urine samples were sent to Dr J. C. Davis at the Department of Endocrine Pathology, Liverpool University, for aldosterone determinations using paper chromatography and a double isotope dilution technique (Lund-Johansen et al., 1966).

Total exchangeable sodium and potassium were determined 24 hours after an intravenous injection of ^{24}Na and ^{42}K, 48 hours after the absorption tests.

Calculations

The results were calculated as described by Shields et al. (1966) using formulas derived by Visscher, Vario et al. (1944) and Visscher, Fetcher et al. (1944), and were expressed as rates of transport for the whole Thiry-Vella fistula, i.e. μEq/10 min. Movement out of the bowel into the body is called 'influx', while movement in the opposite direction is called 'outflux'. The term 'absorption' is used when movement into the blood from the intestinal lumen (influx) is more rapid than movement in the opposite direction (outflux). When the rate of outflux is greater than that of influx, the term 'secretion' is used.

Results

1. *Intravenous infusion of potassium chloride*

a. General effects: After rapid intravenous infusion with potassium (15 mEq in 30 minutes) the plasma concentration of potassium increased, and the electrocardiographs of all the dogs showed peaking of the T waves. Results from one experiment are shown in *Fig.* 1. The blood samples obtained within 5 minutes of completing the infusion usually showed the greatest increases in the plasma concentration of potassium, ranging from 3·2 to 5·9 mEq/l. Accompanying these changes was a small decrease in the plasma concentration of sodium and an increase in that of chloride. The plasma osmolarity also increased. There was no significant increase in the concentration of potassium in the red blood cells or in the mean 24-hour exchangeable potassium measured 48 hours after the infusion. The urinary excretion of aldosterone was never observed to be greater than 1 μg/24 h up to 48 hours after the infusion of potassium chloride.

b. Effect on the intestinal transport of potassium:

i. *Colon*: Immediately after the potassium infusion the rate of potassium secretion into the lumen of colon was increased (*Fig.* 1); the rates of sodium and water absorption usually remained within the range observed in the controls.

Increase in the plasma concentration of potassium (without any change in the initial luminal concentration of potassium) will result in an increase in the concentration difference between plasma and lumen. Our results suggested that there was a relationship between this concentration difference and the rate of potassium secretion. We therefore calculated the

Table I: CORRELATION BETWEEN THE PLASMA/LUMEN CONCENTRATION DIFFERENCE OF POTASSIUM AND THE NET TRANSPORT AND UNIDIRECTIONAL FLUXES OF POTASSIUM, AND THE NET TRANSPORT OF SODIUM AND WATER IN THE COLON

	Dog J			Dog F		
Experiment	No. of tests, *n*	Correlation coefficient, *r*	Significance of this correlation, 2*P*	No. of tests, *n*	Correlation coefficient, *r*	Significance of this correlation, 2*P*
Net transport of potassium						
1	8	−0·82	<0·01	10	0·32	<0·35
2	8	−0·94	<0·001	8	0·15	<0·70
3	12	−0·87	<0·001	11	0·13	<0·70
4	11	−0·94	<0·001	11	−0·84	<0·001
Potassium influx						
1	8	0·60	<0·10	10	0·36	<0·40
2	8	−0·42	<0·40	8	0·48	<0·30
3	12	0·71	<0·01	11	0·90	<0·001
4	11	−0·89	<0·001	11	0·29	<0·40
Potassium outflux						
1	8	0·98	<0·001	10	0·05	<0·95
2	8	0·95	<0·001	8	0·43	<0·30
3	12	0·89	<0·001	11	0·94	<0·001
4	11	0·84	<0·001	11	0·66	<0·025
Net transport of sodium						
1	8	−0·87	<0·005	8	−0·12	<0·70
2	8	−0·67	<0·05	10	0·05	<0·90
3	12	−0·69	<0·01	11	0·47	<0·10
4	11	−0·83	<0·001	11	0·04	<0·90
Net transport of water						
1	8	−0·91	<0·001	10	−0·45	<0·20
2	8	−0·73	<0·05	8	0·06	<0·90
3	12	−0·81	<0·001	11	−0·12	<0·70
4	11	−0·89	<0·001	11	−0·53	<0·10

Table II: CORRELATION BETWEEN THE PLASMA/LUMEN CONCENTRATION DIFFERENCE OF POTASSIUM AND NET TRANSPORT AND UNIDIRECTIONAL FLUXES OF POTASSIUM IN THE ILEUM

	Dog E			Dog P		
Experiment	No. of tests, *n*	Correlation coefficient, *r*	Significance of this correlation, 2*P*	No. of tests, *n*	Correlation coefficient, *r*	Significance of this correlation, 2*P*
Net transport of potassium						
1	5	−0·23	<0·70	8	−0·85	<0·01
2	8	−0·07	<0·90	8	−0·74	<0·025
3	11	−0·29	<0·40	11	0·15	<0·65
4	12	0·47	<0·65	12	−0·66	<0·02
Potassium influx						
1	5	−0·07	<0·95	8	0·89	<0·005
2	8	−0·20	<0·70	8	0·87	<0·005
3	11	0·72	<0·01	11	−0·51	<0·01
4	12	−0·18	<0·60	12	0·92	<0·001
Potassium outflux						
1	5	0·15	<0·90	8	0·93	<0·001
2	8	−0·12	<0·80	8	−0·10	<0·80
3	11	0·68	<0·02	11	0·56	<0·10
4	12	−0·46	<0·10	12	0·86	<0·001

correlation coefficients between potassium secretion and the concentration difference. There was a significant negative correlation in 5 out of 8 experiments in the 2 dogs with a colonic fistula (*Table I*). The correlation was negative because rates of secretion are expressed as negative rates of transport.

The correlations between the concentration difference and the unidirectional potassium movements were also examined. There was a significant positive correlation between the plasma/lumen concentration difference and the potassium outflux in 6 out of 8 experiments in the 2 dogs. Thus, the higher the concentration of potassium on the serosal side of the mucosal cell, the greater was the rate of flux of potassium ions into the lumen. There was no consistent correlation between influx of potassium and its plasma/lumen concentration difference.

In one of the dogs some negative correlations were observed between the plasma/lumen potassium concentration difference and the absorption of sodium and water (*Table I*).

ii. *Ileum*: In the ileum there was poor correlation between the plasma/lumen concentration difference and the secretion of potassium (*Table II*). Only 3 out of the 8 experiments in the 2 dogs showed a significant correlation between the rate of potassium outflux and the plasma/lumen concentration difference. Potassium influx was positively correlated with the concentration difference in 4 out of 8 experiments.

There was no significant correlation between the plasma/lumen potassium concentration difference and the absorption of sodium or water in the ileum.

2. *Effect of raising the intraluminal concentration of potassium on the intestinal transport of potassium*

In an initial series of experiments two test solutions with different concentrations of potassium (4·3 mEq/l, and 11·1 mEq/l) were instilled alternately into the intestinal lumen. The results (*Table III*) showed significantly reduced secretion, or increased absorption of potassium, in 3 out of the 4 dogs when the concentration of potassium in the lumen was increased.

Table III: EFFECT OF AN INCREASED CONCENTRATION OF POTASSIUM IN THE LUMEN ON THE NET TRANSPORT AND UNIDIRECTIONAL FLUXES OF POTASSIUM ACROSS THE MUCOSA

	Colon				Ileum			
	Dog J		Dog S		Dog C		Dog B	
Luminal potassium concentration	No. of tests	Mean±s.e.	No. of tests	Mean±s.e.	No. of tests	Mean±s.e.	No. of tests	Mean±s.e.
Net transport of potassium								
4·3 mEq/l	9	−5·2±0·8	8	−9·9±6·3	9	1·0±3·0	8	−15·2±6·0
11·1 mEq/l	6	1·7±1·7	6	−4·5±6·2	6	46·4±3·0	5	8·7±2·6
Difference of means±s.e.		6·9±1·4		5·4±8·8		45·4±4·4		23·9±7·3
Significance 2*P*, for difference		<0·001		<0·60		<0·001		<0·005
Potassium influx								
4·3 mEq/l	9	5·6±1·2	8	13·3±5·3	9	23·3±2·0		18·3±1·4
11·1 mEq/l	6	11·0±1·6	6	18·4±7·2	6	63·4±2·3		41·7±5·7
Difference of means±s.e.		5·4±1·7		5·1±8·7		40·1±3·0		23·4±5·2
Significance 2*P*, for difference		<0·01		<0·60		<0·001		<0·001
Potassium outflux								
4·3 mEq/l	9	10·8±0·9	8	23·2±1·3	9	22·4±2·0	8	33·5±5·7
11·1 mEq/l	6	99·2±1·7	6	22·9±1·0	6	17·0±2·4	6	33·0±6·7
Difference of means±s.e.		−1·6±1·7		−0·3±1·8		−5·4±3·2		−0·5±9·3
Significance 2*P*, for difference		<0·35		<0·90		<0·10		<0·95

Results given as µEq/10 min.

Table IV: CORRELATION BETWEEN THE PLASMA/LUMEN CONCENTRATION DIFFERENCE OF POTASSIUM AND THE NET TRANSPORT AND UNIDIRECTIONAL FLUXES OF POTASSIUM IN THE PRESENCE OF RAISED INTRALUMINAL CONCENTRATIONS OF POTASSIUM

		Colon				Ileum			
		Dog J		Dog S		Dog C		Dog B	
Experiment	No. of tests, *n*	Correlation coefficient, *r*	Significance of this correlation, 2*P*	Correlation coefficient, *r*	Significance of this correlation, 2*P*	Correlation coefficient, *r*	Significance of this correlation, 2*P*	Correlation coefficient, *r*	Significance of this correlation, 2*P*
Net transport of potassium									
1	15	−0·90	<0·001	−0·27	<0·40	−0·97	<0·001	−0·96	<0·001
2	15	−0·91	<0·001	−0·69	<0·005	−0·98	<0·001	−0·89	<0·001
Potassium influx									
1	15	−0·51	<0·05	0·35	<0·30	−0·97	<0·001	−0·96	<0·001
2	15	−0·84	<0·001	0·42	<0·20	−0·99	<0·001	−0·92	<0·001
Potassium outflux									
1	15	0·74	<0·005	0·66	<0·01	0·45	<0·10	0·77	<0·001
2	15	−0·06	<0·90	0·98	<0·001	0·67	<0·01	0·66	<0·01

These alterations to the net transport of potassium were associated with an increase in potassium influx; potassium outflux did not show any significant change. Net transport of sodium and water was unaltered.

In a subsequent series of two experiments in each dog a range of potassium concentrations from 0·8 to 16 mEq/l were instilled into the lumen. In each experiment 12 absorption tests were carried out with test solutions containing 0·8, 4·0 and 11·0 mEq/l of potassium; 4 tests at each concentration of potassium. A further 3 tests were carried out using a test solution containing 16·0 mEq/l of potassium, giving a total of 15 tests in each experiment. The results are shown in *Table IV*. As the concentration of potassium in the lumen was increased, potassium secretion decreased. There was a significant negative correlation between the rate of net potassium transport and the plasma/lumen concentration difference in 7 of the 8 experiments. There were also significant negative correlations between the plasma/lumen concentration difference and potassium influx in all experiments on the 2 dogs with an ileal fistula, and in 2 of the 4 experiments on the 2 dogs with a colonic fistula. Lower and positive correlation coefficients were observed between the potassium outflux and the concentration difference; these were significant in 6 of the 8 experiments.

The net transport of sodium and water was not significantly changed by raising the concentration of potassium in the lumen of either ileum or colon.

Discussion

The initial increase in the plasma potassium concentration following potassium infusion was limited by the highest concentration of potassium which the dog, and in particular its heart muscle, could tolerate. During this period only a few absorption tests could be performed, because the plasma concentration of potassium fell quickly as a result of its distribution throughout the extracellular space and renal excretion.

An increase in the concentration difference of potassium between the plasma and the intestinal lumen would be expected to increase the transport of potassium down the concentration gradient from the plasma to the lumen, i.e. potassium secretion. This was confirmed in the colon in the present investigation.

More extensive studies of the relationship between potassium transport and the plasma/lumen concentration difference can be performed by increasing the concentration of potassium in the lumen. Under these circumstances there was even better correlation between transport of potassium and its plasma/lumen concentration difference than following the increase in the plasma concentration by intravenous infusion. The luminal concentration of potassium is probably a better estimate of the effective concentration of potassium on the mucosal surface than the peripheral blood concentration is of the effective potassium concentration on the serosal surface.

The rates of unidirectional flux of potassium were also related to the concentration difference between lumen and plasma. When the plasma concentration of potassium was raised, potassium outflux from the colon increased; when the concentration of potassium in the lumen was raised, potassium influx from both colon and ileum increased.

There have been many reports of the good correlation between sodium transport and the sodium concentration difference across the mucosa (Visscher, Fetcher et al., 1944; Curran and Solomon, 1958; Higgins and Blair, 1971; Edmonds and Pilcher, 1972). Sodium absorption increases when the concentration of sodium in the lumen is raised. This is accompanied by an increase in the influx of sodium, but there is no corresponding decrease in the outflux of sodium (Curran and Solomon, 1958; Phillips and Code, 1966; Edmonds and Pilcher, 1972). Results from the present study suggest that potassium behaves in a similar way. In some cases the one-way flux against the concentration gradient was actually increased, although to a lesser extent than the flux down the concentration gradient.

Potassium transport in the colon is usually thought to be passive in nature. Edmonds (1967), who measured potassium net transport and unidirectional fluxes in the rat colon, suggested that potassium influx was by diffusion and that there was no evidence for any exchange diffusion; potassium outflux had two components: active transport and passive diffusion. His results were in agreement with those previously reported by Phillips and Code (1966) in the dog.

The critical concentration of potassium in the lumen is the concentration at which there is no net movement of potassium across the mucosa. The critical luminal concentrations of potassium from the present study are in agreement with those reported by other workers (*Table V*). Phillips and Code (1966) and Edmonds (1967) used the Nernst equation to calculate the luminal concentration of potassium at equilibrium, and showed that the calculated concentrations were in good agreement with the observed concentrations in jejunum and ileum but not in the colon. Similar results were observed by Turnberg (1972); when the critical luminal concentration of potassium approximated to the blood concentration as in the jejunum and ileum, the concentration difference between the plasma and lumen was zero, suggesting that the transfer of potassium occurred by

Table V: RESULTS OF CRITICAL CONCENTRATION OF POTASSIUM IN THE LUMEN FROM THE PRESENT STUDY COMPARED WITH THOSE OF OTHER WORKERS

		Site		
Author	Subject	Jejunum	Ileum	Colon
Phillips and Code (1966)	Dogs	6·1 ($n = 2$)	5·9 ($n = 4$)	17·0
Edmonds (1967)	Rats	—	—	21, 32* ($n = 9$)
Vogel et al. (1969)	Rats	4·6 ($n = 19$)	—	12·3 ($n = 19$)
Turnburg (1972)	Humans	3·5–4·0	4	—
Present study (1975)	Dogs	—	7·2 ($n = 4$)	11·8 ($n = 3$)

* Values for ascending and descending colon respectively.

diffusion down a concentration gradient. However, Turnberg suggested that other processes must be involved in the transfer of potassium by the colon, where there was an appreciable potential difference across the mucosa, and the critical luminal concentration of potassium was much greater than the blood concentration. It is therefore important to measure the potential difference across the mucosa in addition to the unidirectional fluxes of potassium for a complete study of potassium transport in the colon. For this reason the value of many investigations, including the present study, is limited.

Following the intravenous infusion of potassium there was no appreciable increase in urinary excretion of aldosterone measured over 48 hours. The potassium concentration in the adrenal artery is known to have a direct effect on aldosterone production, bypassing the normal renin-angiotensin pathway (Dluhy et al., 1972). Aldosterone production may have increased shortly after intravenous infusion but no excess aldosterone appeared in the urine. Further evidence against the involvement of aldosterone in the increased potassium transport observed in the present study was the lack of any significant effect on sodium absorption.

Although we were unable to produce an increase in the total body potassium, we were able to study the effects of increased concentrations of potassium in the plasma and in the intestinal lumen. These increases would be expected to be similar to those following intravenous and oral administration of potassium respectively.

Unfortunately only one of our dogs was used for both series of experiments. In this dog (which had a colonic fistula) there was a much greater increase in potassium secretion into the lumen following a rise in the concentration of potassium in the plasma, compared with the corresponding decrease in secretion following a similar rise in the concentration of potassium in the lumen (unpublished data). Potassium movement into the body from the intestinal lumen appears to be a relatively slow process. This would explain the greater safety of the oral route for potassium administration.

On the other hand, potassium secretion from the body into the intestinal lumen is a more rapid process, and has been used clinically in the treatment of hyperkalaemia by intestinal dialysis (Schloerb, 1958) and using cation exchange resins. The close relationship between the rate of potassium transport by the intestine and the concentration difference across the mucosa would suggest that whenever the concentration of potassium in the plasma rises, potassium secretion into the gastro-intestinal lumen is increased. Aldosterone does not seem to be involved in this transfer which is probably brought about by simple diffusion.

Acknowledgements

We are grateful to Miss Alma Birch and Mr Gerard Lepts for skilled technical assistance. Rubber catheter balloons were kindly supplied by L.R. Industries Ltd, London. The work was supported by grants from Tenovus and the North West Cancer Research Fund.

References

BERGLUND-LARSSON U. (1956) Determination of small amounts of deuterium oxide in water by infra-red spectroscopy. *Acta Chem. Scand.* **10**, 701–702.

BLACK D. A. K. (1953) Body-fluid depletion. *Lancet* **1**, 353–360.

BLACKMORE D. J., ELDER W. J. and BOWDEN C. H. (1963) Urea distribution in renal failure. *J. Clin. Pathol.* **16**, 235–243.

CLARKE A. M., MILLER M. and SHIELDS R. (1967) Intestinal transport of sodium, potassium and water in the dog during sodium depletion. *Gastroenterology* **52**, 846–858.

CODE C. F. and MCINTIRE F. C. (1956) Quantitative determination of histamine. *Methods Biochem. Anal.* **3**, 49–95.

CURRAN P. F. and SOLOMON A. K. (1958) Ion and water fluxes in the ileum of rats. *J. Gen. Physiol.* **41**, 143–168.

DLUHY R. G., AXELROD L. and UNDERWOOD R. H. (1972) Studies of the control of plasma aldosterone concentration in normal man. II. Effect of dietary potassium and acute potassium infusion. *J. Clin. Invest.* **51**, 1950–1957.

EDMONDS C. J. (1967) Transport of potassium by the colon of normal and sodium depleted rats. *J. Physiol.* (*Lond.*) **193**, 603–617.

EDMONDS C. J. (1969) Kinetics of potassium in colonic mucosa of normal and sodium depleted rats. *J. Physiol.* (*Lond.*) **203**, 533–553.

EDMONDS C. J. and PILCHER D. (1972) Sodium transport mechanisms of the large intestine. In: BURLAND W. L. and SAMUEL P. D. (ed.) *Transport across the Intestine*, A Glaxo Symposium. Edinburgh, Churchill Livingstone, pp. 43–57.

FALBRIARD A., MULLER A. F., NEHER R. and MACH R. S. (1955) Etudes des variations de l'aldostéronuria sous l'effét de surcharges en potassium et de déperditions rénales et extrarénales de sel et d'eau. *Schweiz. Med. Wochenschr.* **85**, 1218–1220.

FORDTRAN J. S. and DIETSCHY J. M. (1966) Water and electrolyte movement in the intestine. *Gastroenterology* **50**, 263–285.

GANN D. S., DELEA C. S., GILL J. R., THOMAS J. P. and BARTTER F. C. (1964) Control of aldosterone secretion by change of body potassium in normal man. *Am. J. Physiol.* **207**, 104–108.

HIGGINS J. T. and BLAIR N. P. (1971) Intestinal transport of water and electrolytes during extracellular volume expansion in dogs. *J. Clin. Invest.* **50**, 2569–2579.

LARAGH J. H. and STOERK H. C. (1955) On the mechanism of secretion of the sodium-retaining hormone (aldosterone) within the body. *J. Clin. Invest.* **24**, 913.

LUETSCHER J. A. and CURTIS R. H. (1955) Aldosterone: observations on the regulation of sodium and potassium balance. *Ann. Intern. Med.* **43**, 658–666.

LUND-JOHANSEN P., THORSEN T. and STOAK K. F. (1966) A comparison of two methods for measurement of aldosterone secretion rate in man. *Acta Endocrinol.* (*Kbh*). **53**, 177–188.

PHILLIPS S. F. and CODE C. F. (1966) Sorption of potassium in the small and the large intestine. *Am. J. Physiol.* **211**, 607–613.

ROSS E. J. (1962) Biological properties of aldosterone. Physiological and pathological implications. *Br. Med. Bull.* **18**, 164–169.

SCHLOERB P. R. (1958) Peritoneal dialysis and the newer methods of intestinal perfusion in renal failure. *Arch. Intern. Med.* **102**, 914–921.

SHIELDS R. (1964) Surgical aspects of the absorption of water and electrolytes by the intestine. *Monogr. Surg. Sci.* **1**, 119–172.

SHIELDS R., MULHOLLAND A. T. and ELMSLIE R. G. (1966) Action of aldosterone upon the intestinal transport of potassium, sodium, and water. *Gut* **7**, 686–696.

SLADEN G. E. G. (1972) Review of water and electrolyte transport. In: BURLAND W. L. and SAMUEL P. D. (ed.) *Transport across the Intestine*, A Glaxo Symposium. Edinburgh, Churchill Livingstone, pp. 14–34.

TURNBERG L. A. (1972) Mechanisms of potassium transport in the human small intestine. In: BURLAND W. L. and SAMUEL P. D. (ed.) *Transport across the Intestine*, A Glaxo Symposium. Edinburgh, Churchill Livingstone, pp. 35–41.

VISSCHER M. B., FETCHER E. S. jun., CARR C. W., GREGOR H. P., BUSHEY M. S. and BARKER D. E. (1944) Isotopic tracer studies on the movement of water and ions between intestinal lumen and blood. *Am. J. Physiol.* **142**, 550–575.

VISSCHER M. B., VARIO R. H., CARR C. W., DEAN R. B. and ERICKSON D. (1944) Sodium ion movement between the intestinal lumen and the blood. *Am. J. Physiol.* **141**, 488–505.

VOGEL G., MEYERING E. and STOECKERT I. (1969) Determination of equilibrium concentrations for some plasma solutes, and studies on the influence of rising Na^+ loads by increasing intraluminal Na^+ concentrations or by increasing perfusion rates on the Na^+ absorption in rat jejunum and colon. *Pfluegers Arch.* **310**, 150–166.

WRIGHT R. D. (1962) Control of secretion of aldosterone. *Br. Med. Bull.* **18**, 159–163.

Br. J. Surg. Vol. 62 (1975) 462–467

Environmental tests of linear flow ventilation for an operating theatre

THE LATE CHARLES C. SCOTT AND THOMAS D. GUTHRIE*

SUMMARY

Criticisms have been levelled against linear air flow operating enclosures because of their alleged physical and biological conditions and the effects of these, both on the surgical team and on the patient's tissues.

THE relevance of airborne contaminants to wound infection has long been suspected, though direct evidence is lacking. Lister in 1871, by introducing the antiseptic spray to sterilize the air above the incision, took the first practical step to eliminate this hazard, and the present-day operating theatre environment has evolved more as a result of enlightened empiricism than scientific planning.

However, wound infection still occurs, and careful experimental work by investigators in many countries has shown conclusively that the air perfusing the exposed tissues may contain many pathogenic bacteria. The same type of bacteria may also escape into the wound through pinholes in the gloves of the surgeon, or may be contaminating the patient's skin through which the incision is made, and the relative importance of these routes in wound infection is difficult to substantiate. In a classic study by Burke in 1963 it was suggested that as much as 68 per cent of wound contamination is by the airborne route. The relevance of linear flow ventilation to the problem of wound infection is unequivocal. By the use of an enclosure ventilated by this system it is possible, for the first time, to perfuse the surgical incision with air which is, for all practical purposes, sterile. Though sepsis is the crucial yardstick by which a linear flow enclosure will be judged, this evidence will take some time to accumulate. In the meantime it is necessary to evaluate the enclosure on other grounds to ensure that it does not make excessive demands on scarce hospital resources or expose patients and staff to unreasonable hazards.

The enclosure

The operating enclosure is a free-standing structure designed in sections to be erected in an existing theatre (*Fig.* 1). It has the following internal dimensions: 3·05 × 3·66 m, with a ceiling height of 2·74 m. The overall height, which includes the filters and fan units, is 3·55 m. Into the basic sections may be fitted a variety of special equipment as required by the type of surgery to be performed.

General illumination is provided by four fluorescent lamps enclosed in dust-sealed translucent covers. The operating lamp is specially designed for use in operating rooms ventilated by the vertical linear flow system; illumination is from six standard operating lamp units mounted in a low profile frame in such a manner as to give as full a range of movements and as effective illumination as do existing operating lamps. Smoke studies showed that it produces no impediment to the flow of filtered air in the wound area. The ventilation of the enclosure is by the vertical linear flow system, already air-conditioned by the existing theatre ventilation system. The air is forced by powerful fans through disposable pre-filters which remove all particles greater than 5 μ into a plenum, or air chamber, the floor of which is entirely composed of high efficiency particulate air filters (HEPA filters), with a pore size of 0·3 μ. The build-up of pressure in the plenum forces the air through the final filter pores in a myriad of parallel air stream lines all over the room simultaneously, then out via peripheral openings in the walls at floor level.

In the investigations described the enclosure was erected in a disused factory, which was being reconstructed for university purposes. An environment more inimical to tests of air cleanliness could hardly be conceived.

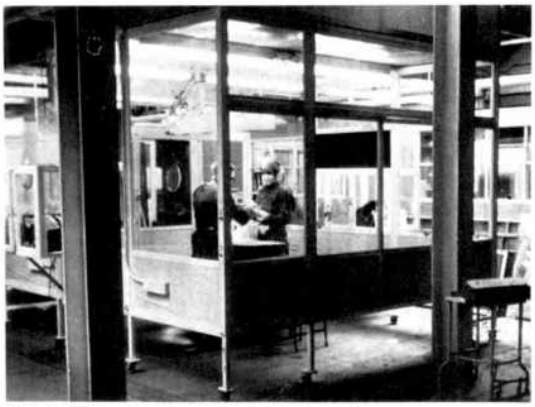


Fig. 1. The free-standing operating enclosure.

Materials and methods

The parameters examined were: (1) air velocity; (2) environmental temperature; (3) tissue drying; (4) air cleanliness, both general and at the incision; (5) noise levels.

1. *Air velocity*

This was measured using a hand-held velometer. By means of a grid, fifteen sampling positions were defined within the enclosure, and the air velocity was measured at three positions; ceiling, head and table height respectively, i.e. 3, 2 and 1 m.

---

* Department of Bacteriology and of Community and Occupational Medicine, University of Dundee.

C. C. Scott died in July 1973 after the tests were completed but before the results were analysed.

2. *Environmental temperature*
The air temperature was measured inside and outside the empty functioning enclosure over a 5-hour period, using a whirling hygrometer to estimate the heat gain from the ventilating and lighting systems.

3. *Tissue drying*
As excessive drying of exposed tissues during surgery would be expected to impair their ability to deal with the local effects of surgical trauma, the impact of the environment on tissues was measured. A whole fresh sheep's liver was obtained from an abattoir. Twelve slices of approximately equal size were cut, each some 9 cm in diameter, so that all the test surfaces were composed of the capsular surface of a lobe. All were weighed on an accurate balance to 0·0001 g and distributed throughout the local environment with equal numbers outside and inside the enclosure. Of those inside the enclosure, half were grouped in the operative area at table height under the operating lamp. Each slice was weighed at half-hourly intervals and the results plotted graphically.

For comparative purposes a similar series of tests was performed in an existing operating theatre ventilated by the turbulent flow system.

4. *Air cleanliness*
The downward flowing stream of clean air might propel contaminants from the head and upper trunk of the surgical team into the wound. A series of tests was designed to quantify total and biologically active particles in this 'critical work site' of the enclosure during a standardized test procedure. For comparison the same tests were repeated in a turbulent flow operating theatre known by previous testing (Scott et al., 1971) to be an efficient one of its type.

In the latter part of the investigation, despite severe theoretical reservations as to the validity of the method, we attempted to enumerate the number of viable particles in the general environment of the enclosure by deploying peripherally situated settle plates on the floor of the enclosure, as described by Charnley (1964).

a. Enumeration of viable particles at the critical work site: To investigate this, a mock incision and a mock operation were devised.

The mock incision was a rectangle of 40 nutrient agar culture plates, each 9 cm in diameter. The total area was therefore 0·56 m^2 and consisted of the whole area of the operating table surface between the two operators (both of whom were fully clothed in conventional theatre garb except for outdoor shoes). The size of the mock incision was chosen to represent a lesion of the whole anterior or posterior surface of the human trunk, e.g. an extensive burn. The exposure necessary for total replacement of the hip joint, which has been much studied in theatre ventilation and is itself among the longer incisions, is approximately one-twentyfifth of this area.

The mock operation lasted 1 hour and was devised to produce repeated arm movements by both operators above the exposed culture plates, and also to oblige them to lean forward repeatedly in both axes of the operating table so that their heads and upper trunk intervened between the illuminated operating lamp and the plates. Each operator took a piece of sterile string from a box at one end of the improvised operating table. The strings were tied together repeatedly, at all times working over the table. After 10 knots, the strings were discarded into a container at the other end of the table. During 1 hour of simulated surgery an average of 500 knots were tied above the mock incision, using hand, arm and trunk movements similar to those used in surgery. The operating lamp was positioned centrally above the table and continuously illuminated. No attempt was made on the grounds of droplet emission to limit conversation which was continuous throughout a rather tedious hour.

Three groups of mock operations were performed in the linear flow enclosure and one in the conventional turbulent flow operating theatre. In the linear flow mock operations the arrangements for each operating session were as follows.

In group 1 the ventilation system was switched on and the enclosure purged for 15 minutes. A set of culture plates was set out on the incision area and systematically uncapped in the direction of the air flow, i.e. from the centre to the periphery. This was found to be a most important detail, and reversing this order invariably led to skin contaminants from the hands lodging on the plates, producing a misleadingly high count. After exposure in the empty enclosure for 1 hour the plates were capped with fresh sterile lids, since lids aggregated together are contaminated on their sterile internal surface by contact with the unsterile outer surfaces of others. The team then gowned up in the enclosure with the ventilation system in operation, and a set of fresh culture plates were exposed in a similar fashion. At the end of the mock operation the plates were capped as before and a fresh series displayed. The ventilation system was then switched off and another mock operation performed.

In group 2 one set of test plates was exposed in the unventilated enclosure, a second set during a mock operation without ventilation and a third set during a mock operation with the ventilation system in action.

In group 3 the procedures were exactly the same as in group 2 except that after the mock operation without ventilation the team changed their sterile gowns, caps, masks and gloves for the operation with the ventilation switched on.

In group 4 the locus was the turbulent flow ventilated operating theatre. One set of plates was exposed in the empty theatre and a second set during a mock operation.

b. Enumeration of total particles: The sampling tube of a Royco automatic particle counter protruded through an aperture in the base of a mock incision so

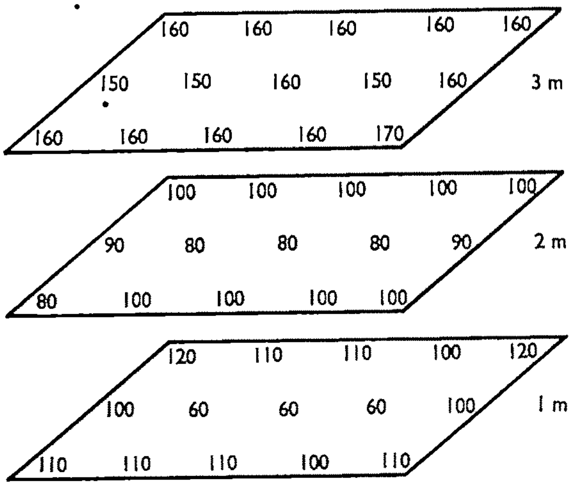


Fig. 2. Linear air flow velocities (ft per min).

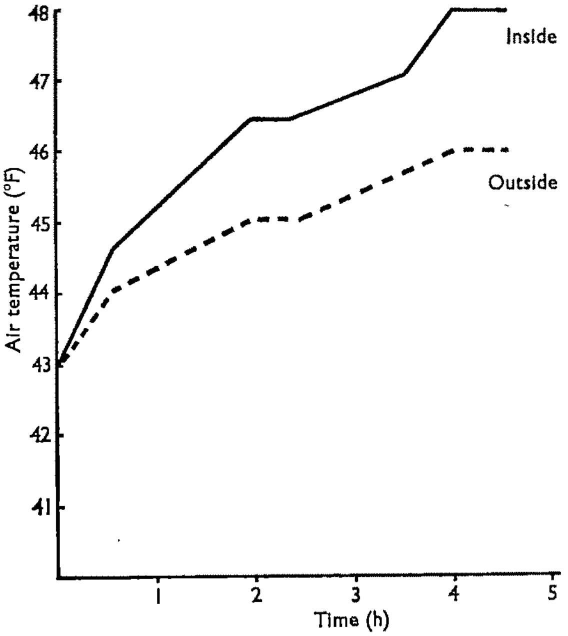


Fig. 3. Environmental temperature.

that the total particle count could be recorded throughout the test period. As the emission, removal and recording of particles are all on-going activities they are illustrated by a range rather than a mean. The Royco particle counter was unavailable at the time the group 4 tests were carried out.

c. *Enumeration of viable particles in the general environment*: Twelve culture plates on the floor at the periphery of the enclosure were uncapped while mock surgery was in progress and remained exposed for 50 minutes. They were then capped and treated similarly to the mock incision plates.

d. *Spatial distribution of the viable particles*: As the distribution of the biologically active particles shed during simulated surgery within the linear flow ventilated enclosure was considered to be of equal importance to their number and identity, all the culture plates were numbered and always arranged in the same order on the operating table. The positions of the two operators were also constant.

e. *Identity of biologically viable particles*: It had been intended to identify all such particles at least to generic level, but this proved impossible in practice because of the very high contaminant counts in the unventilated enclosure and in the turbulent flow operating theatre. In the linear flow ventilated operating enclosure, particular attention was devoted to the examination for *Staphylococcus aureus* as an index of possible human contamination from the team.

All bacterial colonies were examined by Gram's stain. If coccal in morphology, they were tested for catalase and tolerance to salt by subculture on to 6 per cent salt agar for 1 week at 37 °C. If growth occurred they were inoculated into boiled and cooled tubes of Hugh and Liefson's media to disclose fermentative or oxidative properties. If the former, a tube coagulase test was performed.

5. *Noise levels*

The sound pressure levels were recorded using previously calibrated Bruel and Kjaer portable sound level meters (type 2203), incorporating an octave band filter set (type 1613).

Results and discussion

Air velocity (*Fig.* 2)

The velocity of the vertical air flow was found to be less uniform over all the enclosure than had been predicted. It is possible that a contributory cause of this may have been the very considerable number of demonstrations performed using dense clouds of smoke, which may have adversely affected the filter material, although almost certainly defects in the design of the plenum and the enclosure were the main causes. Slight modification of the specifications of the ventilating system can rectify this. Though the velocity of the vertical air flow in the central area was only two-thirds of its design value, smoke tests showed a good flow from the centre of the table to its periphery, and the loci of the viable contaminants at the mock incision confirmed this.

Environmental temperature (*Fig.* 3)

Over a 5-hour period in the empty functioning enclosure a rise of some 1·2 C degrees, relative to the external temperature, was found. A similar series of observations performed within an existing operating theatre confirmed that its air-conditioning system maintained the temperature at 23 °C, compensating for changes in the external temperature, though these were less than 0·6 C degree during the test period. As the linear flow enclosure has no temperature-regulating mechanism and is designed to be used in an existing theatre equipped with these facilities, it does not appear that the heat generated by its use is beyond the regulative capacity of such a system.

Tissue drying (*Figs.* 4, 5)
In the enclosure there was a 3 per cent loss over 4 hours, while in the theatre the corresponding loss was 6 per cent. This suggested that the heat of the theatre lamp was the main cause of the much greater effect in the existing theatre. Though all the tests in the linear flow enclosure were performed at lower environmental temperatures, it should be noted that the light source of the linear flow lamp is identical with that of the theatre lamp. Special features of its design, however, enable it to utilize to the full the cooling power of the greatly increased air turnover of 600 air changes per hour, compared with 20 in the existing theatre. As temperatures in the theatre require the exposed tissue to be irrigated with saline as a routine procedure, these tests do not suggest that the linear flow enclosure is at a disadvantage in this respect.

Air cleanliness (*Tables I, II*)
The total viable particles deposited over 10 hours of mock operating under linear flow ventilation (*Table I*) are seen to have settled on the outer agar plates, i.e. well away from normal-sized incisions.

Performing a mock operation under linear flow ventilation resulted in an average of 6 viable particles per hour being deposited on the 0·6 × 0·9 m mock incision, whereas with no ventilation the viable particulate deposition was increased by a factor of approximately 100 (*Table II*, group 1). Performing a mock operation under linear flow ventilation wearing the same gown etc. as had been used during a mock operation without ventilation increased the deposited viable particulate from an average of 6 per hour to an average of 32 per hour (*Table II*, group 2). The change of gown, cap and mask prior to carrying out a mock operation under linear flow conditions, after performing a mock operation with no ventilation, decreased the viable particle contamination at the work site (*Table II*, group 3). This could be explained by the fact that when no change of clothing was made viable particles adhering to the protective clothing were being flushed off. The deposited viable particles under turbulent flow conditions showed no marked change between an empty theatre and similar conditions with a mock operation being performed (*Table II*, group 4).

As no viable particles were observed in the settle plates situated around the perimeter of the linear flow enclosure, it would appear that the velocity of air passing horizontally outwards around the lower edges of the enclosure is sufficiently high to entrain the viable particulate matter.

Noise levels (*Fig.* 6)
The noise level with all three fans operating is considerably higher than the recommended level for hospitals which is NC 30. Reduction of noise could be

Table I: TOTAL AND VIABLE PARTICLES DURING 10 HOURS SIMULATED SURGERY IN A LINEAR FLOW ENCLOSURE

Type of particle	No.
Saprophytic moulds	23
Bacillaceae, i.e. aerobic spore bearers	19
Micrococcaceae (4 *Staph. albus*)	10
Unidentified bacteria (not human parasites)	8
Total	60

Spatial distribution

0	4(1)	0	4	4	6(2)	3	0
0	0	2	0	1	1	3	0
0	0	0	0	0	0	2	1
0	0	3	2	0	1	1	0
2	2	4(1)	4	2	3	3	2

0·6 m

0·9 m

Central outlined area indicates size of normal incisions.
Numbers of *Staph. albus* given in parentheses.

Table II: TOTAL AND VIABLE PARTICLES AT THE MOCK INCISION UNDER LINEAR FLOW CONDITIONS

Group	Total particles (range/ft³)	Viable particles (mean total/h)
Group 1		
Linear flow ventilation, empty enclosure	15 000–100	<1
Linear flow ventilation, mock operation	100–100	6
No ventilation, mock operation	150 000–3 320 000	576
Group 2		
No ventilation, empty enclosure	3 920 000–4 158 000	78
No ventilation, mock operation	4 138 000–4 512 000	542
Linear flow ventilation, mock operation	42 000–100	32
Group 3		
No ventilation, mock operation	4 576 000–4 960 000	627
Linear flow ventilation, mock operation after change of gown, cap and mask	47 000–100	6
Group 4		
Turbulent flow ventilation, empty theatre	—	53
Turbulent flow ventilation, mock operation	—	56

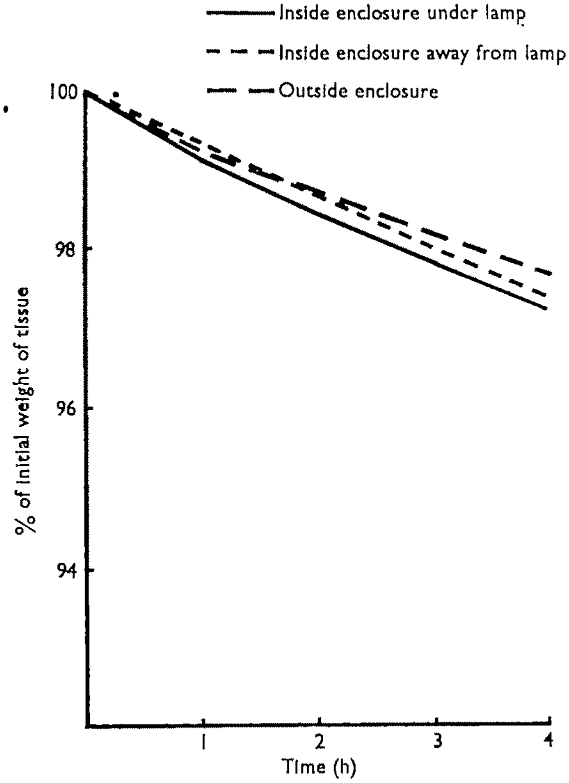


Fig. 4. Tissue drying in linear flow enclosure.

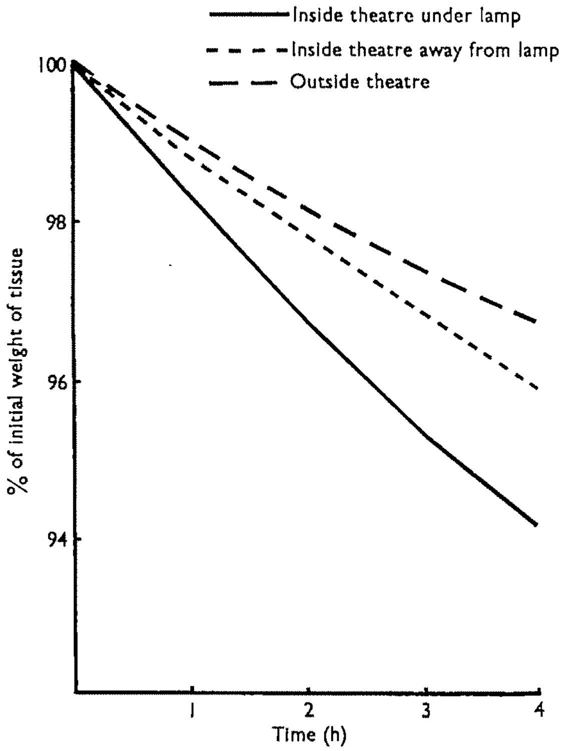


Fig. 5. Tissue drying in operating theatre.

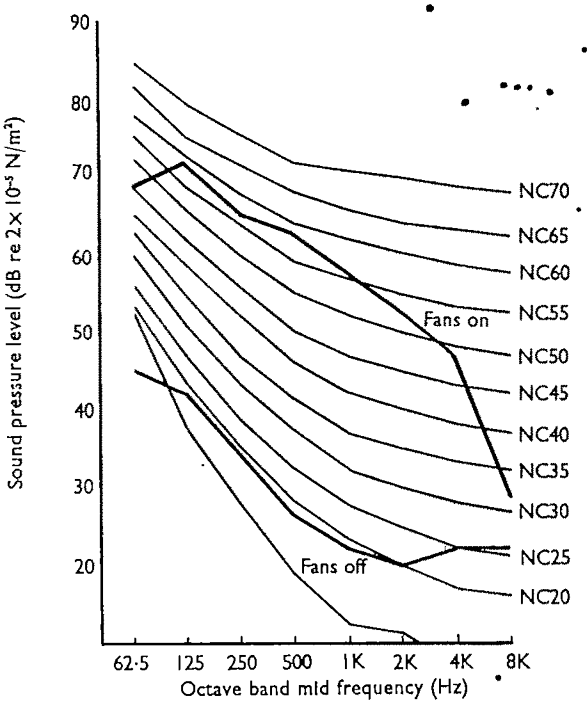


Fig. 6. Noise levels in linear flow enclosure.

achieved by installing quieter running fans and by positioning noise-insulating baffles between the fans and operating team.

Conclusions

This series of tests has shown that many of the fears expressed regarding the conditions to be found in linear flow ventilation in an operating theatre are unfounded.

Changes in temperature were within the regulating capacity of the conventional air-conditioning plant of the theatre within which the enclosure would be installed.

The chief cause of drying of exposed tissue was heat from the theatre lamp, and this was not affected significantly by the increased air flow. The introduction of particulate-free air directed downwards over the patient and operating team at a flow rate of 60–70 linear feet per minute reduced the total particulate matter deposited at the critical work site by a factor of 100.

Most of the surgeons to whom the enclosure was demonstrated showed great interest in the benefits to be expected from its use. Despite the high air turnover (600 air changes per hour), almost all commented on the lack of sensation of air movement and the moderation of the noise level, which they had expected to be excessive.

Acknowledgements

Thanks are due to Mr I. Jacobson and the Nursing Staff of the Department of Neurosurgery, Royal Infirmary, Dundee, for their willing help and co-operation. The staff of the Department of Community and Occupational Medicine assisted in the preparation of the drawings and in typing the manuscript.

References

BURKE J. F. (1963) Identification of the sources of staphylococci contaminating the surgical wound during operation. *Ann. Surg.* **158**, 898–904.

CHARNLEY J. (1964) A clean-air operating enclosure. *Br. J. Surg.* **51**, 202–205.

LISTER J. B. (1871) Address in surgery delivered at the Thirty-ninth Annual Meeting of the British Medical Association. *Br. Med. J.* **2**, 225–233.

SCOTT C. C., SANDERSON J. T. and GUTHRIE T. D. (1971) Choice of ventilating system for operating theatres. *Lancet* **1**, 1288–1291.

'The study of ANATOMY, as it leads to the knowledge of nature and the art of healing, needs not many tedious descriptions nor minute dissections; what is most worth knowing is soonest learn'd, and least the subject of disputes; while dividing and describing the parts, more than the knowledge of their uses requires, perplexes the learner, and makes the science tedious, dry, and difficult.'

CHESELDEN W. (1740) *The Anatomy of the Human Body*, 5th ed., Preface. London, Bowyer.

'I would like to suggest that perhaps there should be in the future a more distinct differentiation of anatomists into those who want to teach medical students and include dissection of the human body as an important part of their curriculum and those who do not. May I remind you what Cardinal John Henry Newman wrote in his book *The Scope and Nature of University Education*? "To discover and to teach are distinct functions; they are also distinct gifts, and are not commonly found united in the same person. He who spends his day dispensing his existing knowledge to all comers is unlikely to have leisure or energy to acquire new. Common sense of mankind has associated the search after truth with seclusion and quiet. The greatest thinkers have been too intent on their subject to admit of interruption; they have been men of absent minds and idiosyncratic habits and have more or less shunned the lecture room and public school".'

DOOLEY D. (Her Majesty's Inspector of Anatomy) *The Arris and Gale Lecture*, 10 May 1972.

Br. J. Surg. Vol. 62 (1975) 468–470

Bilateral idiopathic parotid duct strictures

M. ADISESHIAH*

SUMMARY

Details of 2 patients with idiopathic bilateral parotid duct strictures are presented. The possible aetiology and treatment are discussed.

OBSTRUCTION of Stensen's duct has been attributed to calculus, neuromuscular incoordination, stricture, foreign bodies, mucous plugs and trauma from erupting teeth or ill-fitting dentures (Barsony, 1925; Rose, 1954; Patey, 1965). Two patients have recently been seen with bilateral strictures of the parotid duct in which there was no obvious causative factor. No reports of similar cases have been found in the literature.

Case reports

Case 1: A 43-year-old Asian male presented in April 1973 complaining of intermittent bilateral parotid gland swelling of 1 year's duration. The swelling caused him discomfort; he had learned to massage his glands when swollen and this would result in a gush of saliva inside his mouth with resultant relief of his discomfort. Physical examination revealed a fit young man. Both parotid glands were slightly distended and tender. The teeth, gums and orifices of the parotid ducts looked normal. The patient was able to demonstrate the emptying of his parotid glands by massaging. A gush of saliva appeared at the duct orifice. Subsequently the gland felt normal again.

Plain X-ray of his parotid glands and ducts did not reveal a calculus. Parotid sialography was performed and a film of the right side is shown in *Fig.* 1. There is a narrowing of the terminal 2 cm of the parotid duct. Proximally there is uniform dilatation of the main duct, but the small ducts and acini appear normal. Similar changes were found on the left side.

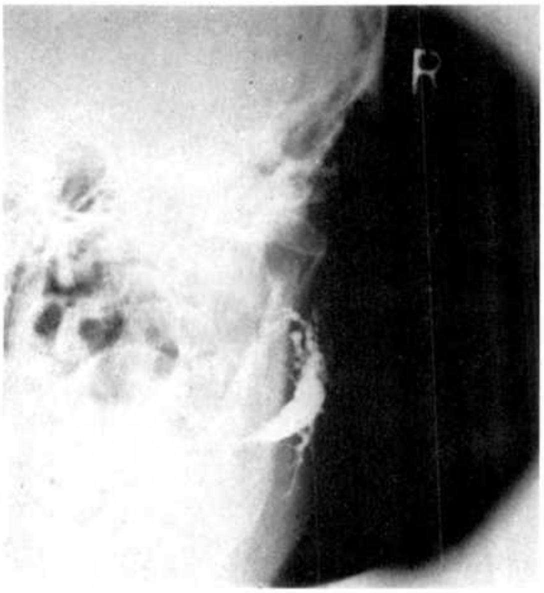


Fig. 1. *Case* 1. Right parotid sialogram showing dilatation of the main duct only with narrowing of the terminal portion.

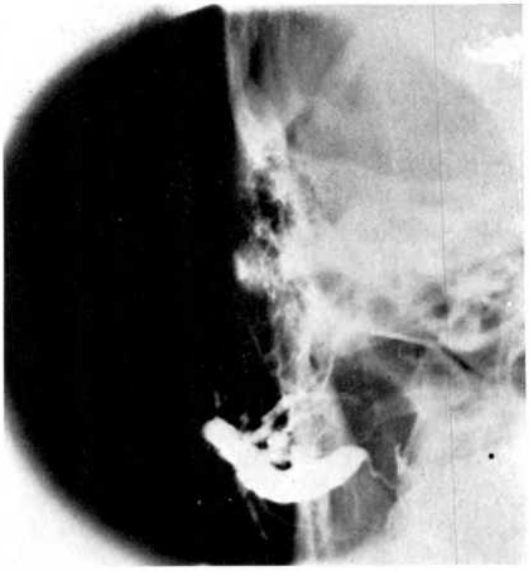


Fig. 2. *Case* 2. Left parotid sialogram showing dilatation of the main duct only with narrowing of the terminal portion.

Case 2: A 29-year-old Asian female presented in October 1972 complaining of intermittent painful bilateral parotid swelling of 1 year's duration. The pain and swelling were invariably present on rising in the morning, and 2–3 hours later there was a sudden gush of saliva accompanied by relief of the pain and swelling. Physical examination revealed a fit young woman with slightly tender swollen parotid glands. The teeth, gums and orifices of Stensen's duct were normal. When the gland was massaged there was a sudden gush of saliva through the orifice with deflation of the gland on that side. The parotid sialogram of the left side is shown in *Fig.* 2. The terminal 0·5 cm of duct is narrow and the proximal part of the main duct is dilated. The small ducts and acini appear normal. Similar changes were seen on the right side.

The patient was treated by dilatation of the terminal portion of the duct with lacrimal duct dilators 3 and 6 months after presentation, but her symptoms remained unchanged.

Subsequently she underwent parotid terminal dochoplasty in which the termination of the parotid duct was slit open up to the dilated portion. The strictured portion was resected on each side and submitted for histological examination. The duct mucosa was sutured to the buccal mucosa with interrupted 4/0 plain catgut sutures. The final result immediately after surgery is shown in *Fig.* 3.

On histological examination both strictures showed an essentially similar nature. The normal pseudocolumnar epithelial lining had undergone squamous metaplasia, deep to which was dense fibrosis with collections of chronic inflammatory cells (mainly lymphocytes and macrophages) without any specific features. No microcalculi or mucous plugs were seen, or any iron pigment which might have indicated previous trauma. This is illustrated in *Fig.* 4. In contrast, *Fig.* 5 shows the appearance of a normal parotid duct (obtained from a 56-year-old man at autopsy). Pseudocolumnar epithelium overlies a narrow zone of loose connective tissue with little

---

* University College Hospital, London.

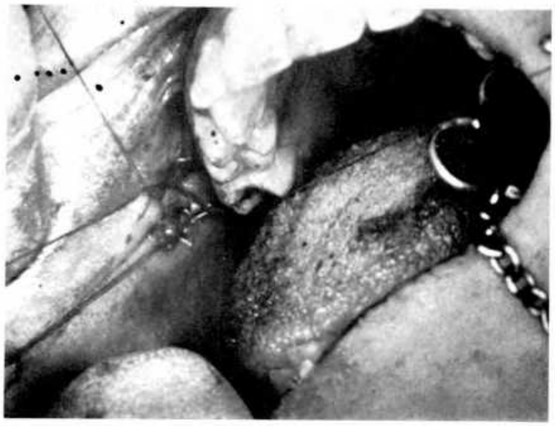


Fig. 3. *Case* 2. Appearance of new right duct orifice at the completion of dochoplasty.

collagen and of scanty cellularity, outside which is buccinator muscle.

Ten days after operation the patient suffered an attack of pain in each parotid region. This was thought to be due to infection and responded well to systemic antibiotic treatment. Ten months after operation she was pain-free. There was a free flow of saliva from each duct orifice.

Discussion

Barsony (1925) described a case of idiopathic bilateral parotid duct obstruction. He suggested that obstruction may be due to neuromuscular incoordination which would result in the main duct failing to release saliva. The lesion may be similar to that seen in the oesophagus in achalasia or in the colon in Hirschsprung's disease. However, in our second patient there was histological evidence of fibrotic stricture.

Rose (1954) described a 'papillary' variety of parotid duct stenosis. This occurred in young people, normally at the time of eruption of the third molar tooth. Food is chewed on the opposite side of the mouth with resultant trauma to the orifice of Stensen's duct on that side. In our patients the onset of symptoms was unrelated to eruption of the wisdom teeth or indeed to trauma. Further, in our patients the condition was bilateral. All of Rose's patients' symptoms cleared up after one or two dilatations, whereas the symptoms of the present *Case* 2 were unrelieved by two dilatations at an interval of 3 months.

Patey (1965) has shown that ductal obstruction may be caused by mucous plugs, the mucus being secreted by glands in the parotid gland and duct itself. However, the sialographic and histological appearances in our patients were not characteristic of the disease that Patey described.

Patey mentioned the triad of obstruction, depression of secretion and infection acting in a viscious cycle that might cause strictures, but in our patients there was no evidence of infection or of diminution of salivary flow. The gush of a large quantity of clear saliva produced on massaging the glands was easily demonstrable. The salivary gushing was recorded on 16-mm moving cine film in *Case* 2 prior to

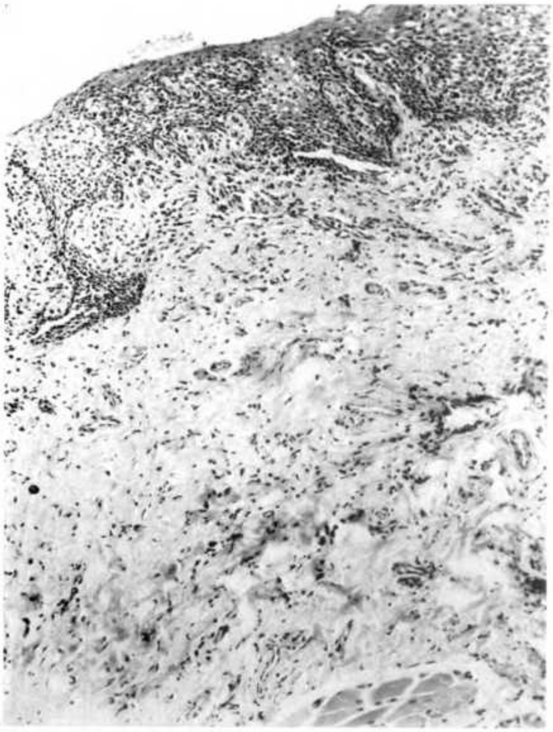


Fig. 4. *Case* 2. Histology of the right parotid duct stricture. Note the dense fibrous tissue extending from the metaplastic squamous epithelial lining to a bundle of skeletal muscle fibres (buccinator). HE. (× 75.)

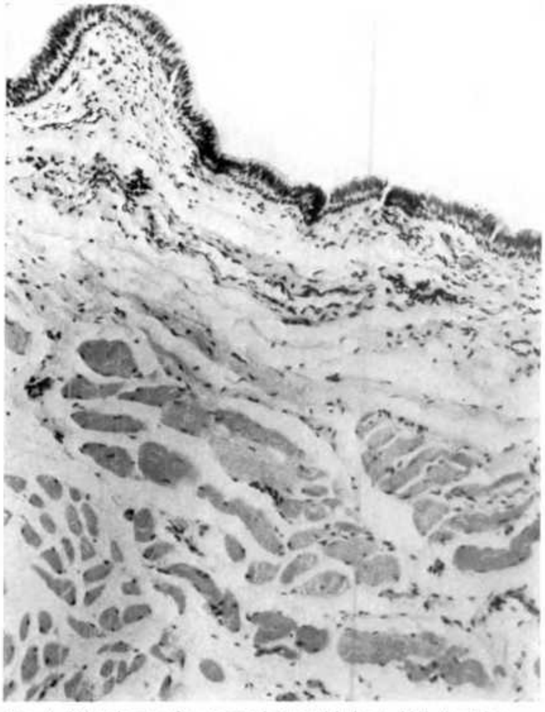


Fig. 5. Histology of a normal parotid duct. HE. (× 75.)

dochoplasty. In recurrent parotitis the secretion is usually viscid, scanty and sometimes contains pus and debris.

The symmetrical nature of the disease suggests that there may be a constitutional and/or dietary factor involved. Both patients rarely chew betel nut and clinically there was no evidence of submucous fibrosis. However, it is possible that a constituent used in spices in Indian cooking may be responsible.

Case 1 obviously required no treatment, having learned to massage his glands and thereby empty them. *Case* 2 was unrelieved by dilatation and had been unable to empty the glands by massage. Hence parotid terminal dochoplasty was performed. This was followed by immediate relief of symptoms; she had one episode of infection which responded to antibiotic therapy. Subsequently she became symptom-free. A possible complication in the long term is the development of ascending parotitis. Prophylactic measures against this include adequate hydration at all times and the use of sialogogues (e.g. citrous-flavoured sweets).

Acknowledgements

My thanks are due to Professor C. G. Clark and Mr D. A. Bailey for allowing me to report on their patients. I would like to express my gratitude to Mr M. J. Hobsley for discussing the problem of idiopathic parotid duct obstruction and to Dr P. M. Sutton and Dr C. Fisher for help with the histology.

References

BARSONY T. (1925) Kasuistische mitteilung. Idiopathischestenongang-dilatation. *Klin. Wochenschr.* **4**, 2500–2501.

PATEY D. H. (1965) Inflammation of the salivary glands with particular reference to chronic and recurrent parotitis. *Ann. R. Coll. Surg. Engl.* **36**, 26–44.

ROSE S. S. (1954) A clinical and radiological survey of 192 cases of recurrent swelling of the salivary glands. *Ann. R. Coll. Surg. Engl.* **15**, 374–401.

DISPRAY 1
Trade Mark
Quick Prep
Chlorhexidine gluconate 0.5% w/v in 70% I.M.S.
Stuart Pharmaceuticals Limited Cheadle, Cheshire.
DISPRAY 2
Hard Surface Disinfectant
Chlorhexidine gluconate 0.02% w/v in 70% I.M.S.
Stuart Pharmaceuticals Ltd Cheadle, Cheshire

DISPRAY 1

TRADE MARK

Quick Prep

Chlorhexidine Gluconate 0.5% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for skin disinfection

'Dispray' 1 Quick Prep.
(formerly known as Hibispray 1)
is an ideal preparation for skin and
hand disinfection in the busy
hospital environment.
At the touch of a button it gives
fast, easy and economical
skin disinfection prior to surgery,
injection or venepuncture.

When colour delineation
is required eg. pre-operatively,
'Dispray' 3 is available
with a red dye.

The 'Dispray' range
combines effectiveness with
convenience and economy.

Instant Availability.
No solutions to prepare.

Easy to use.
No swabs or bottles required.

Quick and Effective.
Rapid bactericidal action.

Efficient Application.
No wasted solutions.

Contents cannot be contaminated.
No rejected solutions.

Long Lasting.
Contents of one can treat 100 sq. ft.

'Dispray' 1, 2, 3.
The Pick of the Bunch
for Disinfection.

DISPRAY 2

TRADE MARK

Hard Surface Disinfectant

Chlorhexidine Gluconate 0.02% w/v
in 70% Industrial Methylated Spirit.

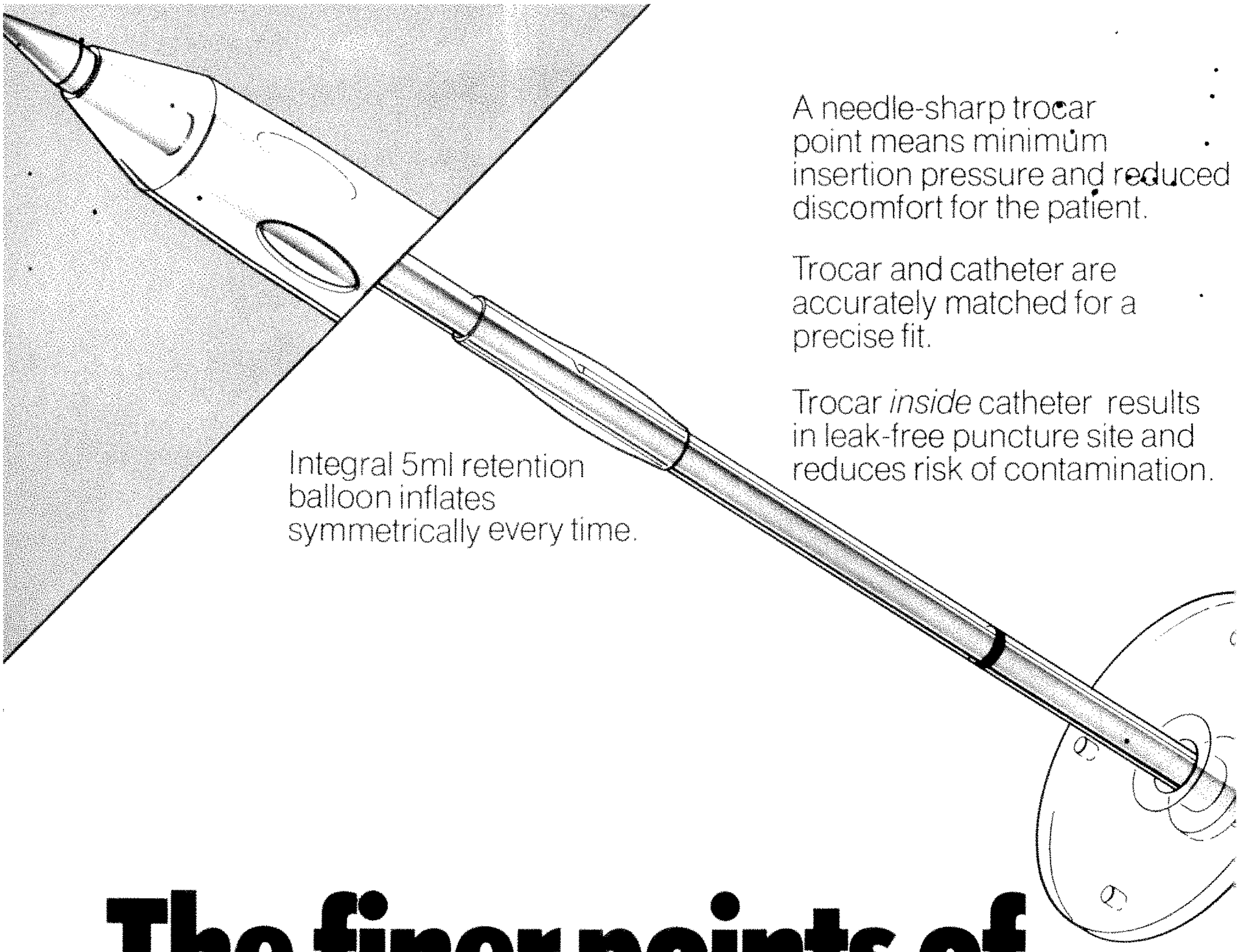
The pick of the bunch for hard surface disinfection

'Dispray' 2 Hard Surface
Disinfectant (formerly known as
Hibispray 2) provides rapid
disinfection of all hard surfaces
throughout the hospital.
Trolleys, cabinets, cupboards,
working surfaces – even footwear,
are rapidly, effectively
and efficiently disinfected.

Further
information
is available
from:

STUART

Stuart
Pharmaceuticals
Limited,
Carr House,
Carrs Road,
Cheadle,
Cheshire SK8 2EG.



A needle-sharp trocar point means minimum insertion pressure and reduced discomfort for the patient.

Trocar and catheter are accurately matched for a precise fit.

Trocar *inside* catheter results in leak-free puncture site and reduces risk of contamination.

Integral 5ml retention balloon inflates symmetrically every time.

The finer points of a suprapubic catheter.

Our precisely engineered trocar and catheter combines maximum efficiency in operation with ease of use.

Check these points and see for yourself.

Sherwood MEDICAL INDUSTRIES

Sherwood Medical Industries Limited, London Road, County Oak, Crawley, West Sussex RH10

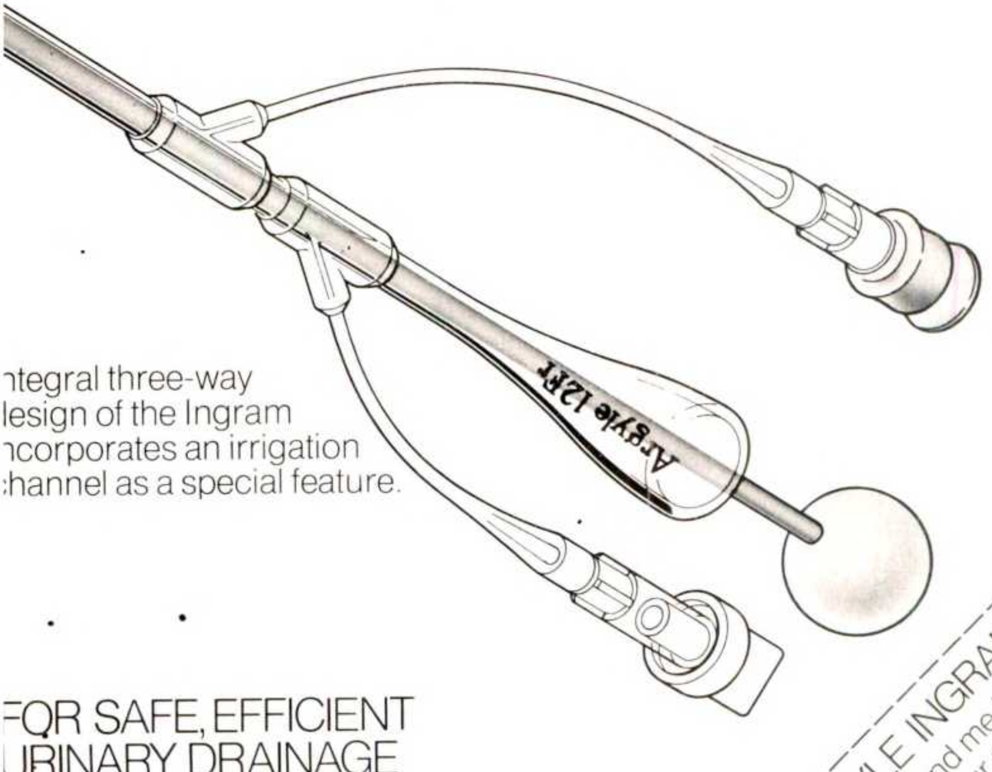
Tip, bevel, eyes. All ultra-smooth, all designed to minimise tissue damage.

Exclusive X-ray opaque Sentinel Line and Eye assists accurate location and positioning of catheter.

Available in both 12Ch and 16Ch sizes. Each unit packed in a convenient peel-back sterile tray.

liding plastic collar enables
atheter to be firmly
xed to maintain position.

nflation channel located inside
he catheter wall. Drainage lumen
is therefore unobstructed.



ntegral three-way
lesign of the Ingram
ncorporates an irrigation
hannel as a special feature.

OR SAFE, EFFICIENT
JRINARY DRAINAGE

ARGYLE

INGRAM TROCAR CATHETER

[illegible] Argyle is a trade mark

THE ARGYLE INGRAM TROCAR CATHETER

Please send me full technical literature ☐

Ask your representative to call ☐

Name (BLOCK CAPITALS PLEASE)

Address

Signature

Your hands are your most important instruments-
it pays to take care of them

The obvious fact that a surgeon's hands are of prime importance to his work was borne in mind when 'Hibiscrub' was formulated. 'Hibiscrub' is designed to keep hands healthy, even after repeated use.

However, the prime importance of a handwash is effectiveness: rapid prolonged bactericidal action against skin bacteria is assured by the presence of the well-proven antiseptic 'Hibitane'.

"These studies have shown that a 4% chlorhexidine detergent solution ['Hibiscrub'] is a potentially outstanding addition to the small list of detergent-disinfectant preparations for the hands of surgeons and nurses, with a greater immediate effect than that obtained with the hexachlorophane or even the iodophor preparations."
British Medical Journal, (1973), 1, 510.

hibiscrub

RAPID BACTERICIDAL SKIN CLEANSER

Contains 'Hibitane' Chlorhexidine Gluconate 4% w/v.

Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

'Hibitane' and 'Hibiscrub' are trade marks.

PH828

Br. J. Surg. Vol. 62 (1975) 471–473

General anaesthesia during early pregnancy

LEO STRUNIN, K. KNIGHTS, J. M. STRUNIN
AND MICHAEL E. WARD*

SUMMARY

General anaesthesia in the early stages of pregnancy may carry an increased risk of embryotoxicity. One hundred and six women scheduled for non-emergency surgery were interviewed preoperatively and their menstrual history taken. Forty-three (41 per cent) were considered to be using adequate contraceptive therapy. Thirty-one (29 per cent) of the patients could have been in the early stages of pregnancy, and of these women, 19 (61 per cent) were undergoing surgery of a minor nature. Simple history taking identified the women 'at risk' and it is suggested that surgery could have been delayed without detriment in many cases.

IT is generally believed that anaesthesia and surgery during early pregnancy carry some risk of spontaneous abortion. The advice usually given, based on clinical experience, is that where surgery is necessary it should be delayed if possible until the second trimester. Animal studies (Smith et al., 1965; Fink et al., 1967) have shown that all the commonly used volatile anaesthetics can cause spontaneous abortion and fetal abnormalities when administered during early pregnancy. The concentrations used in these studies have always been of the order of those during general anaesthesia. Recently, concern has been expressed regarding a possible correlation between low concentrations of volatile anaesthetic agents in the atmosphere of operating areas and the incidence of spontaneous abortion and fetal abnormalities among female operating room personnel (Askrog and Harvald, 1970; Cohen et al., 1971; Knill-Jones et al., 1972). It should, however, be made clear that the evidence for this correlation is entirely circumstantial (Spence, 1973), and the effect of either low or anaesthetic concentrations of volatile anaesthetics in early pregnancy in humans is unknown. It seems that the greatest risk is probably during the early weeks of pregnancy (Shnider and Webster, 1965).

It is not common practice to inquire into a woman's menstrual history prior to general anaesthesia other than for gynaecological surgery. It may be, therefore, that women are exposed unnecessarily to potentially embryotoxic drugs during the earliest stages of pregnancy, indeed before pregnancy is diagnosed. The present study was undertaken to establish the population 'at risk' of undergoing general anaesthesia while pregnant.

Patients and methods

One hundred and six women of childbearing age (14–45 years), scheduled for non-emergency surgery, excluding gynaecology, were visited by one of the authors preoperatively (*Table I*). The patient's menstrual history was taken and the following information obtained:

1. Whether menstrual periods were regular or irregular.
2. The duration of each menstrual period.
3. The interval between menstrual periods.
4. The date of the last menstrual period.
5. Whether they were taking oral contraceptives.
6. Whether there was any chance of pregnancy.

In addition, the nature of the operation to be performed was recorded.

Table I: PREGNANCY RISK GROUPS

Groups		No. of patients		%
Effective contraception				
Oral contraception	32		30	
Hysterectomy	6		6	
Tubal ligation	4		4	
Intra-uterine contraceptive device	1		1	
		43		41
'Pregnancy unlikely'		32		30
'Pregnancy possible'		31		29
	Total	106		

Table II: INTERVAL BETWEEN CALCULATED DATE OF OVULATION AND GENERAL ANAESTHESIA IN 'PREGNANCY POSSIBLE' GROUP

Interval: 10 wk	No of patients: 2
6–9 wk	1
4–5 wk	2
2–3 wk	4
10–13 d	4
5–9 d	3
1–4 d	14
Total	30*

* Pregnancy had been confirmed in 1 patient not included here.

Results

Of the 106 women studied, 43 (41 per cent) were considered to be using adequate contraceptive therapy: 32 (30 per cent) were taking oral contraceptives; 6 (6 per cent) had had a hysterectomy; 4 (4 per cent) had had tubal ligation and 1 had an intra-uterine contraceptive device. Of the remaining 63 (59 per cent) patients, 32 (30 per cent) were calculated on the basis of their menstrual history to be between their last period and ovulation ('pregnancy unlikely' group). Thirty-one (29 per cent) patients were considered to be at risk (*Table II*), since they were at a point in their menstrual cycle where they could have conceived prior to hospital admission ('pregnancy possible' group).

---

* Department of Anaesthetics, King's College Hospital and Medical School, London.

Table III: SURGICAL PROCEDURES CARRIED OUT

Surgery	Effective contra-ception	'Pregnancy unlikely'	'Pregnancy possible'	Total
Dental	18	6	11	35
ENT	6	5	4	15
Breast	8	2	4	14
Abdominal	3	7	2	12
Peripheral	3	5	3	11
Ophthalmic	2	3	2	7
EUA	1	3	1	5
Thyroid	2	1	1	4
Neuro-	—	—	2	2
Thoracic	—	—	1	1
Total	43	32	31	106

On direct questioning, one of the 'pregnancy possible' patients was aware that she was pregnant, but she had reached 28 weeks' gestation and was having an excision of a breast lump. Four other women conceded that they might be pregnant. For 5 patients it was 7 or more weeks since their last period, but of these, one was 15 years of age and her previous period had been her first; 2 others had only within the past 8 weeks terminated regular oral contraceptive therapy. A 27-year-old woman about to undergo dental extractions had waited 10 weeks since her last period and admitted concern that she might be pregnant. However, a pregnancy test performed within the past 5 days was negative. There were 5 other women where more than 4 weeks had elapsed since their last period; of these, one had been in hospital continuously during this time.

Table III shows the operative procedures carried out in the 106 women studied. It can be seen that of the 31 women in the 'pregnancy possible' group, 19 (61 per cent) were undergoing operations of a minor nature which could have been postponed.

Discussion

We have been unable to find any authoritative statement in the world literature concerning the number of pregnant women undergoing anaesthesia. From our investigations, however, it seems clear that women who know or suspect that they may be pregnant have a natural anxiety concerning anaesthesia and surgery. Furthermore, 26 of the 106 women in our series could have been pregnant without being themselves aware of the fact. There are no absolute means of establishing beyond doubt whether or not these women were in the early stages of pregnancy, although more detailed questioning would probably have eliminated a proportion. There are, of course, a number of tests which may be applied. Of these, the Pregnosticon (Organon) or Gravindex (Ortho Pharmaceuticals Ltd) test is the simplest, involving the application of a drop of urine to a slide preparation. An answer, given by the presence or absence of agglutination, is available within 3 minutes. Unfortunately, although only few false positive results are produced there are generally an appreciable number of false negatives. In cases of pregnancy a reliable positive result will not be obtained until 4 weeks after ovulation. This will, therefore, preclude the use of this technique to exclude patients in the very earliest stages of pregnancy when the fetus may be at greatest risk from anaesthetic agents. For this reason such urine testing was not carried out on patients in the present study. Other more sensitive pregnancy tests such as progesterone assay (Yousefnedjadian et al., 1972) or human chorionic gonadotrophin assay (Wide, 1969) are available and will give reliable results after the seventh day following ovulation, but these techniques are slow, expensive and restricted at present to a few research centres. *Table II* shows that even these most sensitive tests of pregnancy would leave more than 14 (45 per cent) of the 31 patients in the 'pregnancy possible' group undetected at the time of anaesthesia and surgery. Therefore, routine testing for pregnancy would not, at present, identify the patients in the earliest stages after conception. Where some departure from a previously regular menstrual cycle draws attention to the possibility of pregnancy, one of the routine pregnancy tests should be carried out, and there may be a case for deferring surgery, where possible, until a conclusively negative result is obtained.

It is regrettable that it is not common practice to ascertain a woman's menstrual history prior to anaesthesia and surgery. It is clear that simple unembarrassing questions can identify a woman who may possibly be pregnant. Since many of the operative procedures were of a non-urgent simple nature, it would seem feasible to delay surgery until the potential risk of pregnancy had passed.

An interesting point concerning the women taking oral contraceptives relates to their anxiety regarding taking their pills in relation to an operation. There seemed to be no clear advice as to whether they should take the pill in the immediate preoperative period and what should be done if they were unable to resume oral contraceptive therapy immediately postoperatively. Our gynaecological colleagues advise us that the correct management should be that where only 1 day is missed it can be compensated for by taking an additional tablet the following day. If 2 or more days are missed, then the advice should be to discontinue oral contraception for 5 days and then commence a new course. It is of course obvious that during the interval conception is possible.

Despite the commonly held view that anaesthesia and surgery should not be carried out during the early stages of pregnancy, our study shows that a substantial number of women who could be pregnant are in fact put at risk. Simple history taking can identify these women, and again our study shows that many of them are scheduled for non-urgent surgical procedures. There may, therefore, be a good case, in the light of the existing evidence concerning embryotoxic effects of volatile anaesthetics, to delay surgery in these instances.

Acknowledgements

The authors would like to thank their surgical colleagues for permission to interview their patients preoperatively, and Mr Julian Elias of the Department

of Obstetrics and Gynaecology, King's College Hospital, for help and advice.

References

ASKROG V. and HARVALD B. (1970) Teratogen effekt af inhalationanaestetika. *Nord. Med.* **83**, 498–500.

COHEN E. N., BELLVILLE J. W. and BROWN B. W. jun. (1971) Anesthesia, pregnancy, and miscarriage. A study of operating room nurses and anesthetists. *Anesthesiology* **35**, 343–347.

FINK B. R., SHEPARD T. H. and BLANDAU R. J. (1967) Teratogenic activity of nitrous oxide. *Nature* (*Lond.*) **214**, 146–148.

KNILL-JONES R. P., RODRIGUES L. V., MOIR D. D. and SPENCE A. A. (1972) Anaesthetic practice and pregnancy. Controlled survey of women anaesthetists in the United Kingdom. *Lancet* **1**, 1326–1328.

SHNIDER S. M. and WEBSTER G. M. (1965) Maternal and fetal hazards of surgery during pregnancy. *Am. J. Obstet. Gynecol.* **92**, 891–900.

SMITH B. E., GAUB M. L. and MOYA F. (1965) Investigations into the teratogenetic effects of anaesthetic agents: the fluorinated agents. *Anesthesiology* **26**, 260–261.

SPENCE A. A. (1973) Contamination of air by anaesthetics. *Ann. R. Coll. Surg. Engl.* **52**, 360–361.

WIDE L. (1969) Early diagnosis of pregnancy. *Lancet* **2**, 863–864.

YOUSEFNEDJADIAN E., FLORENSA E., COLLINS W. P. and SOMMERVILLE I. F. (1972) Radio-immunoassay of 17-hydroxyprogesterone. *J. Steroid Biochem.* **3**, 893–901.

Br. J. Surg. Vol. 62 (1975) 474-479

Renal transplantation in the unimmunosuppressed pig: an abnormal response

JOHN TERBLANCHE, ROSEMARY HICKMAN AND C. J. UYS*

SUMMARY

A series of 82 kidney allografts and autografts in unimmunosuppressed pigs surviving for longer than 5 days has been compared with a previously reported series of 24 unimmunosuppressed pig kidney allografts. In the previous series 40 per cent survived for longer than 20 days. In the present series only 2 per cent of 55 transplants performed in cross-bred pigs obtained from different farms survived for longer than 20 days. The major causes of death were unrelated to rejection, principally gastric ulcer bleeding. In the further 16 transplants between different pure-bred animals (thereby ensuring genetic disparity) the ulcer incidence was lowered by a gastro-enterostomy, and 12 per cent survived for longer than 20 days. Histological assessment of rejection in the latter group revealed 20 per cent with minimal rejection, and 60 per cent in which rejection was considered insufficient to account for the death of the animals. Based on the evaluation of 95 unimmunosuppressed pig kidney allografts in both series, it is concluded that a wide and unpredictable range of survival time occurs. Therefore the pig kidney allograft model is an unsatisfactory model in which to study immunosuppressive régimes. Also the unimmunosuppressed pig appears to show less evidence of kidney allograft rejection than the dog, irrespective of genetic disparity. It is tentatively suggested that this might be a lesser manifestation of the unexplained phenomenon of minimal rejection of liver allografts noted in unimmunosuppressed pigs.

IN a previous paper a series of 24 kidney allografts in unimmunosuppressed pigs was reported. Survival in 40 per cent of these animals was longer than 20 days and in 25 per cent longer than 40 days (Terblanche et al., 1973). On the other hand, skin allografts were rejected normally. This and earlier reports documented protracted survival following liver transplantation in the unimmunosuppressed pig (Dent et al., 1971a; Spilg et al., 1971; Spilg et al., 1972). We have also suggested that the pig is unique in its ability to tolerate vascularized organ allografts (Terblanche et al., 1973). Reports from other laboratories have shown the immunological effect of pig liver allografts, resulting in prolonged survival of simultaneous transplants of skin or kidneys (Calne et al., 1969), and the potentiating effect of portal venous drainage on pig kidney allografts (Mazzoni et al., 1971).

It has also been reported that the pig cellular immune response is more susceptible to modification than that of other animals (Perper et al., 1971). These findings require further elucidation and are at present being investigated in detail in our laboratory. The first phase of the investigation was a detailed study of unimmunosuppressed pigs with kidney allografts which is reported in this paper. In some pigs, biopsies were performed at 10 days, and the histology compared with subsequent autopsy specimens, since a reduction in the cellular manifestations of rejection had been noted in serial biopsies from unimmunosuppressed liver transplants (Dent et al., 1971a). A small series of autografts was also performed to investigate the biochemical and histological response to the transplant procedure itself, and to act as a control for the allograft experiments. Previous studies have shown that some features possibly attributable to rejection in unimmunosuppressed pig liver allografts also occur in autografts, and may be due either to the operation or to subsequent complications, especially infection (Dent et al., 1971a).

Materials and methods

Kidney allo- and autografts were performed in 100 unimmunosuppressed pigs weighing between 15 and 20 kg and aged between 35 and 50 days. Only the 82 pigs which survived longer than 5 days have been included in the analysis, as the 18 earlier deaths were due to technical failures. *Table I* shows the experimental design. Eleven autografts (group A) were performed to obtain baseline control data. The 71 allografts were divided into group B (55 experiments) where cross-breed Large White/Landrace pigs obtained from different farms were used, and group C (16 experiments) where different pure-bred pigs were used as recipient and donor in each experiment in an attempt to ensure genetic disparity. A gastro-enterostomy was performed in the last 9 pigs in group B and all the animals in group C in an attempt to reduce the incidence of bleeding gastric ulcers (unpublished data).

Anaesthesia and drugs

All the animals were given a commercial feed ('creep' meal) until the day before operation and then starved for 24 hours preoperatively, with access only to water (Dent et al., 1971b). Anaesthesia was induced with halothane, and maintained through an endotracheal tube with oxygen, nitrous oxide and halothane given by intermittent positive pressure ventilation. A catheter was inserted into the external jugular vein and used to administer 300–400 ml Ringer's lactate in 10 per cent invert sugar intraoperatively and to obtain

---

* Departments of Surgery and Pathology, the Medical Research Council Liver Research Group, University of Cape Town, and the Liver Clinic, Groote Schuur Hospital, Cape Town, South Africa.

Table I: EXPERIMENTAL DESIGN SHOWING SURVIVAL ANALYSED ACCORDING TO PROCEDURE AND ISCHAEMIC TIME

Group	No. of pigs	Procedure	Ischaemic time Length	No. of pigs	Mean ± s.d. (min)	Biopsy (no.)	Mean survival (d)
A	11	Autograft	L	4	61 ± 8	2	18 ± 3
			S	7	28 ± 4	5	25 ± 5
		Allograft*					
B	55	i. No gastro-enterostomy	L	17	56 ± 10	3	14 ± 2
			S	29	26 ± 4	8	10 ± 3
		ii. Gastro-enterostomy	S	9	29 ± 6	0	11 ± 2
C	16	Allograft† with gastro-enterostomy	S	16	33 ± 10	0	13 ± 7

* Large White/Landrace cross-breed pigs with donor and recipient obtained from different farms.

† The donor and recipient pig in each experiment was of a different pure breed, viz. Large White, Landrace or Large Black.

postoperative blood samples. During the operation each animal was heparinized with 2 mg/kg and received 0·5 g chloromycetin and 600 mg crystalline penicillin, as well as 2 mg furosemide to stimulate urine flow, and 100 mg sodium bicarbonate during the period of aortic clamping to compensate for the associated metabolic acidosis. No blood transfusion was administered. In addition, in 19 animals in group B (i) iron–dextran complex was administered intravenously in an attempt to prevent the anaemia noted in previous allografts.

The donor procedure

A similar operative technique to that described in 1971 by Golby and White was used with several specific modifications. Two pigs were anaesthetized simultaneously in the allograft experiments, each donating its left kidney for orthotopic transplantation.

Using full sterile precautions, the abdomen was opened through a long midline incision. In each pig a right nephrectomy was performed and this kidney discarded. The left renal artery was dissected out to the aorta and the renal vein dissected beyond the confluence of tributaries to ensure an adequate lumen for anastomosis. Care was taken to preserve the lumbar artery and vein which branched from the aorta and renal vein at this site. Ligation of the lumbar artery resulted in hindlimb paralysis in 3 pigs, as also reported by Golby and White, while careless incision of the lumbar vein at the time of kidney removal led to problems in subsequent venous anastomosis. The nerves around the aorta were preserved where possible, as severance appeared to be a contributing factor in hindlimb paralysis. In most cases the large lymph ducts around the aorta were opened during dissection.

After heparinization, the kidney was removed, taking a Carrell patch of aorta with the renal artery and leaving a defect in the aorta which was cross-clamped above and below the site. The kidney was submerged in cold saline without perfusion. The kidney ischaemia time (*Table I*) depended upon the availability of one or two surgical teams for the allografts. Where both transplants were performed by one operator, one kidney was immersed in saline at 4 °C until the first procedure had been completed, and was then transplanted into the other pig (long ischaemia time). This was simulated in 4 of the autografts.

The recipient procedure

The donor kidney was placed in the left renal fossa. The renal artery was anastomosed to the defect in the recipient aorta using the Carrell patch with continuous 4/0 silk, and a direct renal vein to renal vein anastomosis was performed with continous 5/0 silk. Mean renal ischaemia times ranged from 26 to 61 minutes (long or short ischaemic time groups as shown in *Table I*). A direct ureter to ureter anastomosis was performed just below the renal pelvis using interrupted 6/0 silk. In most instances the branch from the renal artery to the upper ureter was preserved with the donor kidney. Urine excretion usually commenced immediately. In the animals in group B (ii) and group C an anterior gastro-enterostomy was performed using two layers of 3/0 catgut in an attempt to prevent gastric ulceration. The posterior peritoneum over the kidney was closed with 2/0 catgut and the abdomen closed in layers with 0 chromic catgut and a subcuticular nylon suture.

Postoperative course

All the animals received intravenous infusion for 24 hours and then recommenced oral feeding. The antibiotics (chloromycetin and pencillin) were continued for 5 days, and blood samples were taken for a week, thereafter at 10 days and then at weekly intervals. Renal biopsies were performed as an open procedure under minimal halothane anaesthesia between 9 and 11 days postoperatively in 18 animals in groups A and B (*Table I*). A full autopsy was performed as soon as possible after death, but always within 18 hours.

Results

Survival

A review of the allografts in groups B and C (*Table I*) showed that neither differences in ischaemic interval nor the addition of a gastro-enterostomy altered the mean survival time in this group of unimmunosuppressed pigs. The survival times of the present allografts have been compared in *Table II* with a previously reported group of 24 unimmunosuppressed pigs of the same or different breeds in which surprisingly prolonged survival was obtained (Terblanche

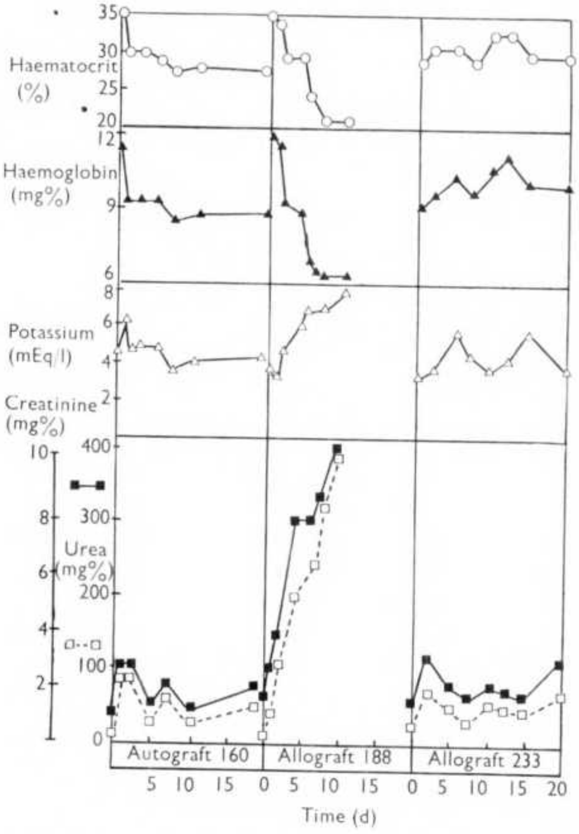


Fig. 1. The typical biochemical and haematological changes following an autograft, an allograft with severe rejection (pig no. 188) and an allograft with mild rejection (pig no. 233) are shown in representative graphs.

et al., 1973). In the cross-bred pigs obtained from different farms in group B 18 per cent survived for more than 14 days, 2 per cent for more than 20 days and none for more than 40 days, while in group C, where transplants were performed in different pure-bred pigs to ensure genetic disparity, the survival was longer, viz. 25 per cent for 14 days, 12 per cent for more than 20 days and 6 per cent for more than 40 days. This latter unexpected finding was at least partly due to death from complicating bleeding gastric ulcers in group B (*vide infra*). In this present large series of transplanted pigs the protracted survival seen in our previous series was not achieved (50 per cent longer than 14 days, 40 per cent over 20 days and 25 per cent over 40 days).

Biochemistry

Representative biochemical patterns from an autograft, a severely rejecting transplant and a minimally rejecting transplant are shown in *Fig.* 1. In the autograft animals a mild early elevation of serum urea and creatinine occurred, probably as a result of ischaemic damage. This elevation returned to normal within 10 days. No marked late fall in haemoglobin was noted. In animals undergoing severe rejection a sharp rise occurred in serum urea, potassium and creatinine within 2–3 days of transplantation. This rise persisted and the animals appeared able to tolerate very high levels for several days. Urine output was not measured. A marked fall occurred in haemoglobin and packed cell volume, but no significant changes were seen in leucocyte or platelet counts. In the animals surviving longer with little evidence of rejection, minimal elevation occurred in serum urea, creatinine and potassium and no significant change occurred in haemoglobin or haematocrit.

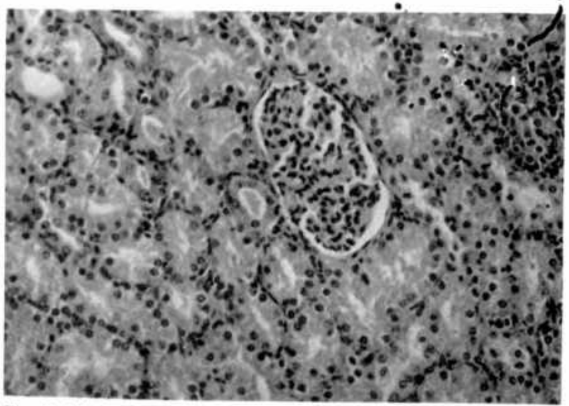


Fig. 2. Minimal evidence of rejection (histological category 1). This illustrates minimal rejection in which only slight tubular degeneration and scanty focal infiltration of mononuclear cells are evident. HE. (× 106.)

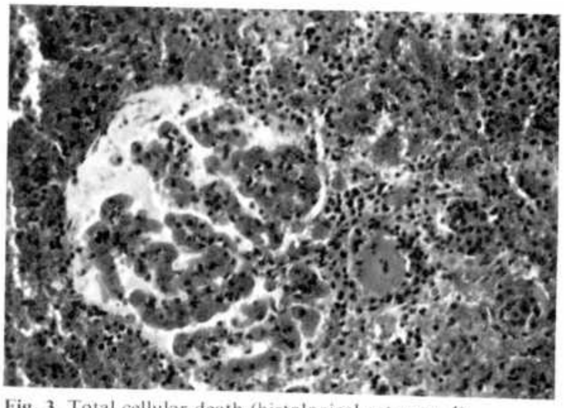


Fig. 3. Total cellular death (histological category 4). Complete haemorrhagic infarction involving all renal elements, accompanied by moderate interstitial infiltrate of mononuclear and polymorphonuclear leucocytes. HE. (× 106.)

Histology

The histological material was reviewed independently by the three authors and grouped according to evidence of cellular rejection. The findings could be grouped into four patterns (*Figs.* 2, 3). The patterns and mean survival times are shown in *Table III*. In group B no difference in survival was noted, despite variable patterns of rejection. In fact, only in the 20 per cent of animals in group C showing minimal rejection was survival prolonged to a mean of 24·6 days. In the 18 animals in which a biopsy was performed the features noted were similar to the subsequent pattern at autopsy. No resolution was noted, but unfortunately

Table II: PERCENTAGE SURVIVAL IN GROUPS B AND C COMPARED WITH PREVIOUSLY REPORTED DATA

Survival (d)	Allografts, present series Group B ($n = 55$)	Group C ($n = 16$)	Allografts, previous series ($n = 24$)
>14	18	25	50
>20	2	12	40
>40	0	6	25

Table III: HISTOLOGICAL FINDINGS IN GROUPS B AND C

	Group B		Group C	
Histological pattern	%	Mean survival time ± s.d. (d)	%	Mean survival time ± s.d. (d)
1. Minimal evidence of rejection	7	9·3 ± 2	20	24·6 ± 5
2. Significant rejection	48	10·6 ± 4	40	10·3 ± 3
3. Cortical necrosis with rejection	39	10·2 ± 2	40	9·3 ± 2
4. Total cellular death	6	9·3 ± 1	0	0

Table IV: COMPLICATIONS NOTED IN ALL THE ANIMALS REPORTED IN THIS STUDY

		Group B ($n = 55$)		
Complication	Group A ($n = 11$) autograft	(i) ($n = 46$)	(ii) ($n = 9$)	Group C ($n = 16$)
Rejection only	—	22	6	11
Pneumonia	4	2	0	3
Ureteric leak	3	3	0	0
Gastric ulcer	2	16	3	0
Others including haemorrhage after biopsy, peritonitis, renal vein thrombosis and long P.M. interval	2	3	0	2

in all the biopsy cases no more than 5 days elapsed between biopsy and autopsy. No firm conclusion can therefore be drawn about possible spontaneous reversal of rejection as has been seen in liver allografts in unimmunosuppressed pigs (Dent et al., 1971a; Terblanche et al., 1973). The four histological patterns shown in *Table III* are described below.

1. *Minimal evidence of rejection* (*Fig.* 2): The kidneys showed minimal changes of cellular rejection. This manifested as an almost complete absence of interstitial cellular response, or as inconspicuous focal interstitial mononuclear cell infiltrates of both the cortex and medulla which tended to occur perivascularly. Vascular and glomerular changes were generally absent. In a few pigs the mononuclear infiltrate was more severe, and in these the vascular endothelial cells were prominent and the glomeruli showed segmental cellularity largely due to epithelial and mesangial cell proliferation. The tubules were remarkably normal except for hydropic degeneration which was unrelated to the severity of the interstitial infiltrate or the glomerular or vascular changes. In 2 kidneys there were changes of acute pyelonephritis.

2. *Significant rejection*: A constant feature in these kidneys was a more pronounced patchy interstitial infiltrate of mononuclear cells. In many the infiltrates became confluent and presented as sheets of pyroninophilic mononuclear cells in an oedematous interstitium. The infiltrate also included plasmacytoid cells. The tubules showed changes varying from severe degeneration to necrosis, but tubular regeneration indicative of post-necrosis was also apparent. Once again hydropic degeneration was a notable feature. Even the severely damaged epithelium appeared hydropic, suggesting that this change had existed before the onset of necrosis. In many of the tubular lumina, aggregates of polymorphonuclear cells occurred. In a few cases there were areas of patchy interstitial capillary haemorrhage, focal and segmental glomerular necrosis or atrophy (suggestive of earlier necrosis) and vascular lesions consisting of endothelial cell swelling, mononuclear cell infiltration of the media and, rarely, fibrinoid necrosis. Occasionally the glomerular tufts showed generalized increased cellularity.

3. *Cortical necrosis with rejection*: These biopsies were characterized by patchy areas of haemorrhagic infarct-like necrosis of both cortex and medulla, which alternated with areas of viable parenchyma showing pronounced cellular infiltrates, as well as notable tubular, glomerular and vascular changes. In the areas of necrosis all tissue elements showed necrosis of varying duration associated with prominent interstitial haemorrhage. In these areas there was evidence of an interstitial infiltrate which included many polymorphonuclear as well as the usual mononuclear cells. Often all cellular elements had disintegrated and only poorly stained cell outlines were evident, which were mingled with chromatin debris. The polymorphonuclear cells were more obvious at the borders of the necrotic areas. The viable areas always occurred at the junction of the cortex and medulla and included variable amounts of both these tissue components. The changes observed in the non-necrotic areas were similar but more severe than those described in the preceding group. Necrosis of the large arterial radicles was prominent and these frequently contained thrombi.

4. *Total cellular death* (*Fig.* 3): Complete haemorrhagic infarction of the entire kidney was noted in these biopsies. In some this had occurred recently, while in others even the cell outlines of the necrotic tissues were no longer distinguishable and the necrosis was of longer duration. In every respect the appearances were similar to those described in the necrotic areas of the kidneys in the third category, and differed only in that the necrosis was total instead of subtotal.

Complications

The major complications which caused death in these animals are shown in *Table IV*. In the autografts the principal causes of death were pneumonia, ureteric leak and gastric ulceration. In the animals of groups

B and C rejection was often present in addition to the apparent cause of death. However, this rejection was mild and frequently considered insufficient to be the sole cause of death (histological categories 1 and 2). The principal complication in group B (i) was fatal gastric ulceration, constituting 35 per cent. These ulcers were large, as previously noted after liver transplantation (Dent et al., 1971b), and death resulted from haemorrhage or occasionally perforation. In 48 per cent of cases no cause of death other than rejection could be found, even though this was often only mild or moderate (histological categories 1 and 2). It is of interest that in animals in group B (ii) gastro-enterostomy did not prevent ulceration completely and one-third still apparently died from this complication. In group C using the same procedure no ulcers occurred, and the major cause of death was rejection, although once again this was often mild. In 20 per cent there was severe pneumonia.

Discussion

In previous studies of kidney transplantation in the pig few experiments without immunosuppressive manœuvres have been described, and also few data of biochemical and histological changes under these circumstances are available. The unique response of the pig to liver transplantation with minimal rejection (Calne et al., 1969; Dent et al., 1971a) makes such a study essential. The present detailed study was designed to investigate the response of the unimmunosuppressed pig to kidney allografts. The survival and biochemical and histological features were specifically studied and compared with our previously reported small series in which prolonged survival had been noted (Terblanche et al., 1973).

In the group of 71 allografts surviving for longer than 5 days a wide range of survival times was noted. The differences in survival could not be correlated with ischaemic intervals. There was some decrease in mortality in the latter part of the series when gastro-enterostomy was performed to prevent gastric ulceration, which was a complication in many of the animals. Haemorrhage from these ulcers and pneumonia contributed significantly to the shortened survival times in the present series. This is particularly important as in 55 per cent of group B (transplantation between cross-bred pigs) and 60 per cent of group C pigs (transplantation between different pure-bred pigs) histological features of rejection did not appear severe enough to have caused death (histological categories 1 and 2).

Biochemical investigation of autografts showed a minimal rise in urea and creatinine levels for 4 days after transplantation, probably related to the operative procedure. In allograft animals undergoing marked rejection this rise continued rapidly and persisted until death. It was accompanied by a fall in haemoglobin and haematocrit irrespective of whether gastric ulceration was present. Hence, at least some of the haematological changes were attributable to rejection, although no significant changes were noted in total leucocyte or platelet counts. In animals without biochemical evidence of rejection no similar changes were noted in haemoglobin or haematocrit, and histology showed mild to moderate rejection.

The histological patterns fell into four categories. None showed the severe cellular infiltrate noted in unimmunosuppressed dog kidney allografts (Porter, 1964). In the autograft animals death was caused by gastric ulceration, pneumonia and ureteric leaks, and no features of infection, or features similar to those of rejection, were seen. This is unlike the liver autografts previously reported from our laboratory, where infection (ascending cholangitis) confused the histological picture (Dent et al., 1971a). The 55 per cent of animals in group B and 60 per cent in group C which showed rejection, apparently insufficient to cause death, also showed only moderate biochemical changes. In these animals death was attributed to pneumonia or gastric haemorrhage or other undetermined causes.

Hence, the response of the unimmunosuppressed pig to kidney allotransplants is not as violent as that reported in the dog (Porter, 1964), and 10 per cent of animals survive beyond 20 days and some as long as 1 year, with evidence of chronic low grade rejection at autopsy.

The major histocompatibility locus for pigs has recently been demonstrated by mixed lymphocyte culture and lymphocytotoxicity allo-antisera (Vaiman et al., 1970; White et al., 1973), and the survival of renal allografts has been shown to be related to serological identity. In another more recent study in our laboratory no serological identity was detected in pigs of different breeds (Parker et al., 1975), yet in group C allografts between different pure-bred pigs 12 per cent survived beyond 20 days. In our previously reported series the mean survival time for different breed transplants was more than 20 days. Furthermore, in our laboratory 85 per cent of liver allografts in unimmunosuppressed cross-bred non-litter mates showed prolonged survival of up to 2 years, and in some, resolution of histological rejection has been noted (Terblanche et al., 1973).

The present results indicate that the cellular immune response of the pig to renal transplantation is variable, even without the addition of immunosuppressive agents as used by others (Perper et al., 1971; Symes et al., 1972), and further intensive studies are required of the anomalous response of this animal to a vascularized organ graft. It is concluded that the wide range of rejection response and the variable sporadic long term survival obtained in the pig kidney allograft model make it unsuitable for investigation of immunosuppressive régimes.

Acknowledgements

The continued interest and support of Professor J. H. Louw, Head of the Division of Surgery, University of Cape Town, are gratefully acknowledged. Experiments were conducted with the assistance of the staff of the J. S. Marais Surgical Laboratory; biochemical determinations were made by Mesdames J. Green, J. Fourie, C. Rose Innes and P. van Heerden, and histological specimens were prepared by Mrs S. Carstens and Mr S. E. Abbott.

Financial assistance was received from the Medical Research Council of South Africa, the CPA, the Staff Research Fund of the University of Cape Town and the Chris Barnard Fund.

References

CALNE R. Y., DAVIS D. R., HADJIYANNAKIS E., SELLS R. A., WHITE D., HERBERTSON B. M., MILLARD P. R., JOYSEY V. C., DAVIES D. A. L., BINNS R. M. and FESTENSTEIN H. (1970) Immunosuppressive effects of soluble cell membrane fractions, donor blood and serum on renal allograft survival. *Nature (Lond.)* **227**, 903–906.

CALNE R. Y., SELLS R. A., PENA J. R., DAVIS D. R., MILLARD P. R., HERBERTSON B. M., BINNS R. M. and DAVIES D. A. L. (1969) Induction of immunological tolerance by porcine liver allografts. *Nature (Lond.)* **223**, 472–476.

DENT D. M., HICKMAN R., UYS C. J., SAUNDERS S. J. and TERBLANCHE J. (1971a) The natural history of liver allo- and autotransplantation in the pig. *Br. J. Surg.* **58**, 407–413.

DENT D. M., UYS C. J., HICKMAN R., SAUNDERS S. J. and TERBLANCHE J. (1971b) Gastric ulceration complicating experimental liver transplantation in the pig. *J. Surg. Res.* **11**, 289–296.

GOLBY M. and WHITE H. J. O. (1971) The operation of orthotopic renal allografting in the pig, and its complications. *Br. J. Surg.* **58**, 287–288.

MAZZONI G., DI MARTINO C., MELIS M., DEMOFONTI A., VALLI A., FRANCESCONI M. and PELLEGRINI S. (1971) Organ transplantation in the pig with different portal and caval venous drainage. *Eur. Surg. Res.* **3**, 62–71.

PARKER J. R., HICKMAN R. and TERBLANCHE J. (1975) Immunological studies in pig organ transplantation using the mixed lymphocyte culture technique. *Transplantation.* In the press.

PERPER R. J., BOWERSOX B. E. and VAN GORDER T. J. (1971) Prevention of rejection of porcine renal allografts. *Transplant Proc.* **3**, 488–493.

PORTER K. A. (1964) Pathological changes in transplanted kidneys. In: STARZL T. E. (ed.) *Experience in Renal Transplantation.* Philadelphia, Saunders, pp. 300–306.

SPILG H., UYS C. J., HICKMAN R., SAUNDERS S. J. and TERBLANCHE J. (1971) Successful liver transplantation after 6–8 hour storage using a simple hypothermic immersion technique. *Transplantation* **11**, 457–460.

SPILG H., UYS C. J., HICKMAN R., SAUNDERS S. J. and TERBLANCHE J. (1972) Twelve-hour liver preservation in the pig using hypothermia and hyperbaric oxygen. *Br. J. Surg.* **59**, 273–276.

SYMES M. O., GOLBY M. G., JAFFE W. P., JAGO R. H., LAI T. W. L. C., LUCKE J. N., LUCKE V. M., OLSON I. A., PONSFORD F. M. and WHITE H. J. O. (1972) Observations on the effect of horse anti-pig leucocyte sera in suppressing the rejection of renal allografts in pigs. *Transplantation* **13**, 218–223.

TERBLANCHE J., HICKMAN R., SHIPPEL R. M., DENT D. M., SPILG H., IMMELMAN E. J., DU TOIT E., UYS C. J. and SAUNDERS S. J. (1973) Prolonged survival of vascularised organ allografts in unimmunosuppressed pigs. *Transplant. Proc.* **5**, 749–754.

VAIMAN M., RENARD C., LA FAGE P., AMETEAU J. and NIZZA P. (1970) Evidence for a histocompatibility system in swine (SL-A). *Transplantation* **10**, 155–164.

WHITE D. J. G., BRADLEY B., CALNE R. Y. and BINNS R. M. (1973) The relationship of the histocompatibility locus in the pig to allograft survival. *Transplant. Proc.* **5**, 317–320.

Br. J. Surg. Vol. 62 (1975) 480–486

Injuries caused by rubber bullets: a report on 90 patients

R. MILLAR, W. H. RUTHERFORD, S. JOHNSTON AND V. J. MALHOTRA*

SUMMARY

The injuries in 90 patients caused by rubber bullets are described. There was 1 death and 17 people in the series had permanent disabilities or deformities. In 41 patients the injuries necessitated admission to hospital. One fatality outside this series is known. Injuries to the head and neck were frequent and severe.

IN July 1970 in Northern Ireland the British Army introduced a new missile, the rubber bullet. This article describes the injuries to 90 patients caused by this missile. Cases were collected by contacting all the hospitals in Belfast and Londonderry and asking for details about rubber bullet injuries. Most of the serious and many of the minor injuries were seen personally by one or more of the authors.

Ballistic details

The rubber bullet is a blunt missile which is intended to administer a painful slap severe enough to deter stone throwers but not severe enough to cause major injuries. It is the mechanical descendant of the wooden club or baton. The first attempt to modify a baton so that it could be fired was in Hong Kong. This missile was made of wood, and the Army spoke of 'firing baton rounds'. For the civil disturbances in Northern Ireland the wooden missile was replaced by one made of hard rubber. The Army has continued to speak of 'firing baton rounds', but civilians have always referred to the missiles as 'rubber bullets'.

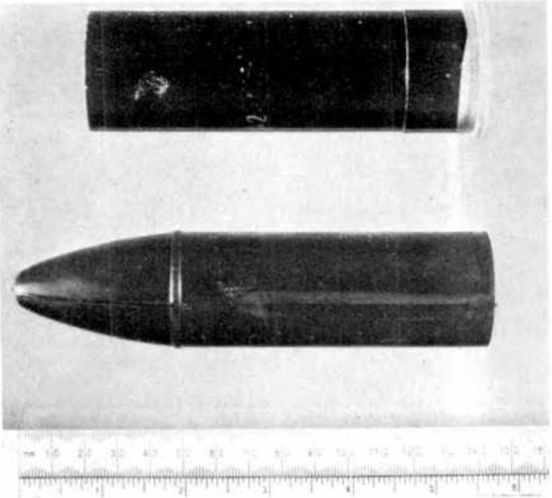


Fig. 1. Rubber bullet with its cannister.

When the rubber bullet was designed it was decided to use it for firing in a weapon already in production. The weapon chosen was designed originally for firing canisters of CS gas, and is in current use by the Royal Ulster Constabulary for this purpose. The army refers to this weapon as the 'RUC riot gun'. A rubber bullet can also be fired from the Verey pistol.

The term 'bullet' gives a correct impression of shape, but not of size—it is 15 cm long, 3·5 cm in diameter and weighs 135–140 g. It is mounted in a canister with a charge of 55 grains in the base (*Fig.* 1). It fits loosely into the barrel of the riot gun and is highly unstable in flight. The muzzle velocity is 73 m/sec, but with tumbling movement and high wind resistance it loses energy very rapidly. The loose barrel and tumbling flight are also responsible for its inaccuracy. At 18 m it is difficult to hit a target 2 m in diameter.

Patients

Table I shows the sex distribution. It is noteworthy that while women formed 33 per cent of the total series, they represented only 10 per cent of the patients who required admission to hospital. Of the less serious cases where admission was not necessary, just over 50 per cent were women.

Table II shows the age distribution. The youngest patient was 7 years old and the oldest 67.

Table III shows the anatomical site of the injuries. In 5 cases two areas of the body were injured, giving 95 sites in 90 patients. The great majority of these lesions were on the anterior aspect, a few were lateral and only two were on the posterior aspect, one on the back of the neck and the other on the back of a leg.

Injuries to specific organs

1. *Skin and soft tissues*

Of the 90 patients, the records note the absence of obvious damage to the skin and soft tissues in only 2 or 3 cases. By far the most common lesion was a bruise, and this was usually elongated, in some cases giving a striking reproduction of the shape of the bullet (*Figs.* 2, 3, 4). In 2 cases it was noted that the bruise was circular, presumably from an end-on impact. The typical shape of the bruise was somewhat less evident in face and head injuries. Injuries to the face characteristically caused gross swelling and bruising of the cheek, lips and eyelids, with or without abrasions and lacerations (*Figs.* 5, 6). There was one scalp laceration with no skull fracture, but in one case of very severe comminuted skull fracture there was no overlying laceration.

---

* Royal Victoria Hospital, Belfast.

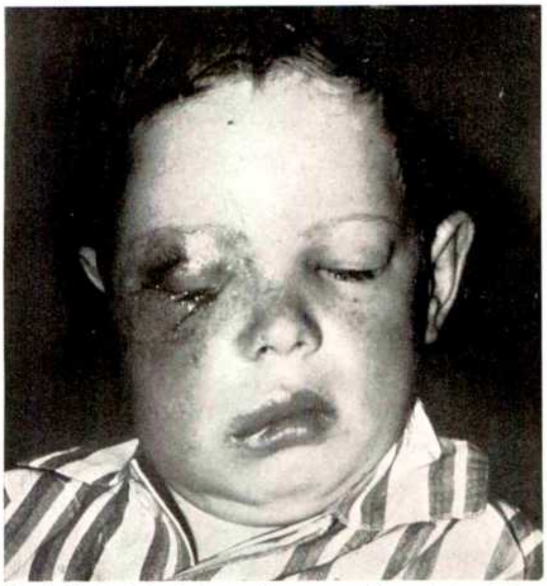


Fig. 5. Typical face injury with gross swelling of the orbit and undisplaced malar fracture.

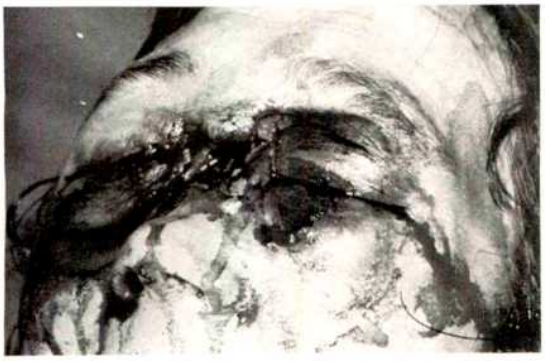


Fig. 6. Severe injury with compound fracture of the nose, maxillary fracture and destruction of both eyes.

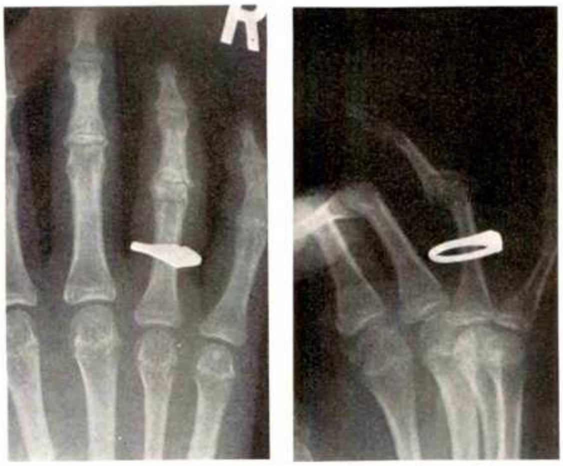


Fig. 7. Fracture of the base of the middle phalanx of the right ring finger.

common injury was a fracture of the malar and/or nasal bones. Blow-out fracture of the orbit also occurred. In one case the force was sufficient to displace the maxilla laterally and in another the mandible was fractured and displaced. One patient had a depressed fracture in the frontotemporal region combined with massive shattering of the whole vault of the skull (*Fig*. 8). Fractures due to frontal impact were less common. In several cases the nasal bones were comminuted and flattened. In one of these there was an associated fracture of the frontal bones with a cerebrospinal fluid leak for several days. In another the whole maxilla was driven downwards and backwards and there were associated fractures of the malar bones and nose and a blow-out fracture of the left orbit (*Figs*. 6, 9). In this patient both eyes were ruptured. Another patient, who suffers from osteogenesis imperfecta, had a direct impact on the frontal bones, resulting in a depressed fracture and an extradural haematoma which required surgical intervention.

3. *Eyes and ocular adnexa*

Twenty-four cases had injuries to the eyes or adnexa, 4 of which were bilateral; 10 right eyes and 18 left were involved (*Table V*). Two (8 per cent) of the patients were women. This is similar to the percentage of women among inpatients (10 per cent) rather than in the total series (33 per cent). In comparison with injuries to other sites of the body there was a similar age range but more cases occurred in the older age groups. All except 4 were treated as inpatients, with an average duration of 10 days' hospitalization.

Gross ecchymosis, periorbital and orbital oedema were a feature of all the cases (*Fig*. 5). In 7 cases bruising and lacerations of the lids alone were involved and these all had good visual results and no permanent disability. Thirteen cases had associated facial or skull fractures of which 6 required surgical reduction.

Twenty globes were injured, contusion accounting for 12. Severe visual loss was caused by traumatic cataract in 2 and by choroidal tears and retinal scarring in the macular region in 6. There were 8 ruptured globes all of which resulted in blindness; 4 had to be excised. A bilateral case who was severely injured at short range is shown in *Fig*. 6. Apart from visual loss, permanent disability was caused by anosmia in 3 cases and a marked change of facial appearance in 3 cases.

4. *Brain*

In 7 patients there was loss of consciousness. In 2 this was very brief—a matter of a few minutes—and in another 2 there was amnesia for less than 1 hour. Of these 4 mild cases, one was associated with a fractured mandible and the other 3 had no bony injuries. The 3 more severe cases of brain injury were associated with skull fractures. One of these made a complete recovery with no disability, one recovered well in spite of the damage to a frontal lobe noted at operation and the third patient died (*Fig*. 8). At operation he was noted to have gross cerebral oedema. It is noteworthy that no unconsciousness or amnesia was noted in any of the

Table I: SEX DISTRIBUTION

	Outpatients		Inpatients		Total	
Sex	No.	%	No.	%	No.	%
Men	24	49	37	90	61	67
Women	25	51	4	10	29	33
Total	49	100	41	100	90	100

Table II: AGE DISTRIBUTION

			Total	
Age (yr)	Outpatients	Inpatients	No.	%
0–9	2	3	5	6
10–19	30	28	58	64
20–39	9	2	11	12
40+	7	7	14	16
Unknown	1	1	2	2
Total	49	41	90	100

Table III: SITE OF INJURY

		Inpatients		Total	
Site	Outpatients	No.	%	No.	%
Head and neck	18	33	80	51	54
Chest	14	7	18	21	22
Abdomen	3	1	2	4	4
Arms	8	0	0	8	8
Legs	11	0	0	11	12
Total	54	41	100	95	100

Table IV: FACE AND SKULL FRACTURES

Site	Displaced	Undisplaced	Total
Malar	5	7	12
Maxilla	2	0	2
Orbital floor	5	0	5
Nose	4	7	11
Mandible	1	1	2
Skull	3	0	3
Total	20	15	35

In one case a bruise on the calf of the leg later broke down with considerable sloughing of the subcutaneous tissues. This was skin-grafted and healed well. One bruise over the lower chest wall and epigastrium increased in size and on the fifth day measured 30 cm and was fluctuant; 150 ml of thin, bloodstained fluid, full of fat globules, were removed, presumably the result of traumatic fat necrosis.

2. *Bony injuries*

The only fracture in a long bone of the limbs was in a finger (a dislocation of a proximal interphalangeal joint with fracture of the base of the middle phalanx) (*Fig.* 7). In this case the finger was pinched between the rubber bullet and a wall. In the trunk the only fractures were of the ribs. Of 24 chest injuries, 9 of which required admission, rib fractures occurred in only 2 cases.

By contrast, fractures of the face and skull were relatively common. There were no fractures among 18 injuries to the head where admission was judged unnecessary. Of 33 patients with head injuries who were admitted, 21 patients had sustained fractures of the face and skull bones. Several patients had fractures at more than one site, making a total of 35 fractures. *Table IV* sets out the details of these fractures.

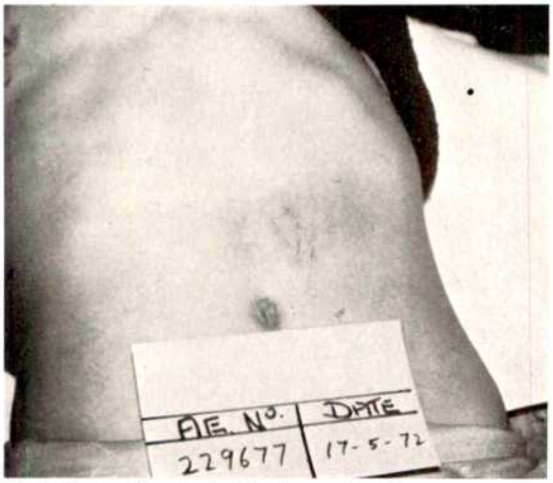


Fig. 2. Typical longitudinal bruise on the abdomen.

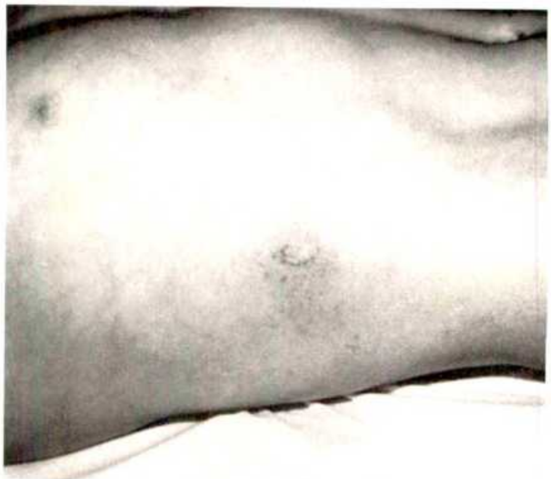


Fig. 3. Circular bruise over right lower ribs.

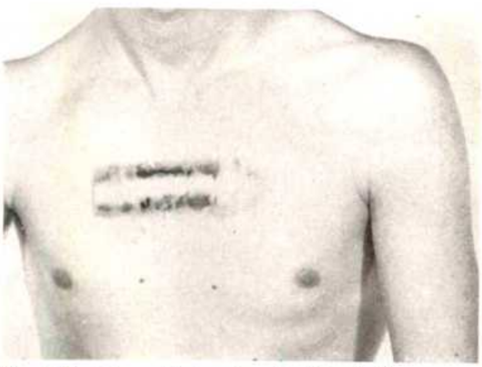
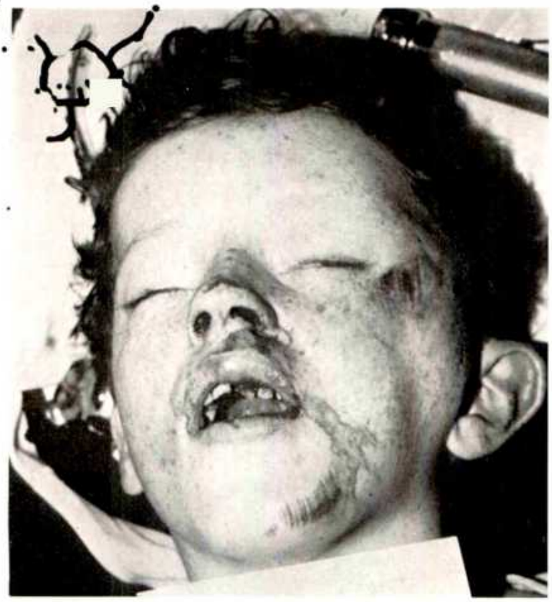


Fig. 4. Bruising with imprint of rubber bullet.

Fractures of the facial bones and skull did not show any unusual features as compared with those due to other types of blunt trauma. The fracture patterns reflect the direction and momentum of the missiles and the inherent lines of weakness in the skeleton of the face. In most cases the impact was from the side and a



a

Table V: EYE INJURIES

Injury	Visual results Good (>6/12)	Poor (6/36–3/60)	Blind (<3/60)	Excised	Total
Contusion and laceration of lids	8	—	—	—	8
Contusion of globe	4	5	3	—	12
Ruptured globe	—	—	4	4	8
Total	12	5	7	4	28

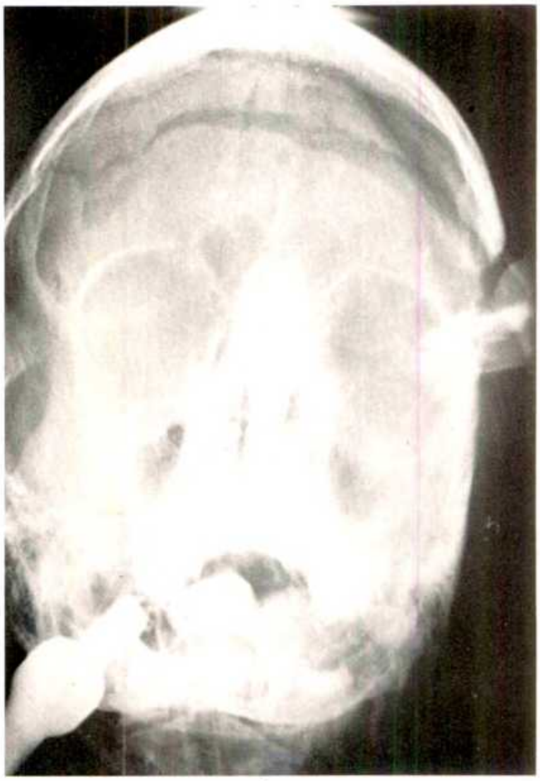
No cases fell into the 'fair' category (6/18–6/36).

cases with eye injuries, and that only one facial bone fracture was associated with amnesia.

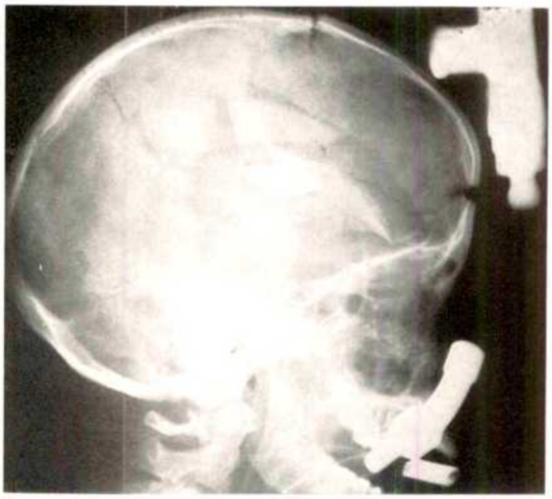
5. *Lungs*

Of the 9 cases of injuries to the chest which were admitted to hospital, 7 had injuries of the lung (the other 2 had subdiaphragmatic injuries). Three of these have been reported elsewhere (Shaw, 1972). None of the chest injuries treated as outpatients had lung damage visible on X-ray.

The clinical picture in the lung injury cases was striking. Within minutes, if not seconds, of injury the patient coughed up blood. In some cases the notes state that it was not frank blood but very frothy sputum which was either streaked with blood or completely red. In every case so presenting, X-rays taken in the casualty department revealed an opacity in the lung (*Fig.* 10). The patients were distressed and dyspnoeic but not cyanosed. Some caused sufficient anxiety to be sent to the intensive care unit for a short period. Within a few days there was striking improvement in the clinical condition. Follow-up has been difficult but some opacities have remained for 4 weeks. In 1 case a small pneumothorax accompanied the lung contusion and in 2 cases there were fractured ribs. In the 3 cases in which the $P\text{o}_2$ was recorded it varied between 45 and 76 per cent (breathing air).



b



c

Fig. 8. *a*, Circular bruise lateral to the left eye. Anteroposterior (*b*) and lateral (*c*) X-rays of the skull.

6. *Liver*

There was 1 case of injury to the liver. This 13-year-old boy was admitted with a circular bruise over the right lower chest wall (*Fig.* 3). There was tenderness and guarding in the right upper quadrant, and it was

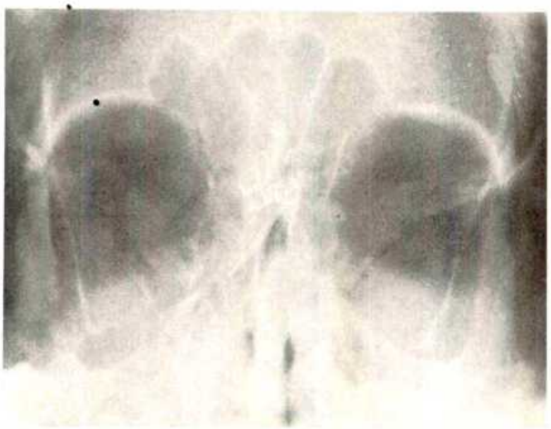


Fig. 9. Postoperative X-ray showing fractures of the nose, maxilla, orbital floor and malar bone of the patient shown in *Fig.* 6.

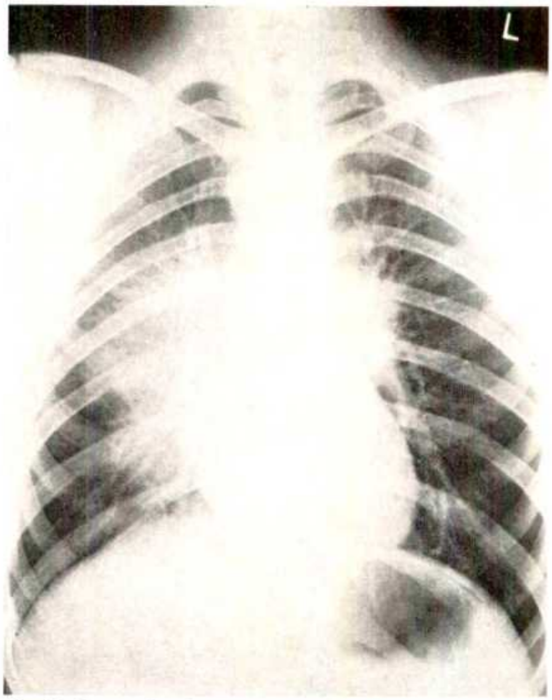


Fig. 10. X-ray showing contusion of the lungs of the patient shown in *Fig.* 4.

thought possible that he might have blood in the peritoneum. However, it was decided to treat him conservatively. Two days after admission he developed jaundice which was 4·0 mg per cent at maximum. The serum glutamic oxalo-acetic transaminase, lactic dehydrogenase and alkaline phosphatase were all markedly elevated. An intravenous cholangiogram was normal. The condition resolved spontaneously and he was discharged in good health on the twelfth day after injury.

7. *Spleen*

In 1 case, a 16-year-old boy, the spleen was ruptured. On initial examination the only positive finding was slight tenderness in the lower left costal area. X-ray revealed no fracture of the ribs. Two hours later he developed pain and tenderness in the abdomen and general signs of blood loss. At operation there was a tear on the diaphragmatic surface of the spleen. Splenectomy was followed by an uncomplicated recovery.

8. *Intestine*

The single case recorded was a 67-year-old man who was struck on the abdomen. On examination there was a circular bruise in the left iliac fossa and marked tenderness, guarding and rebound tenderness. At laparotomy there was a perforation of the jejunum. Bruising was noted around the perforation and at multiple sites in the jejunum. The perforation was sutured and the patient made an uneventful recovery.

Range of bullets

Details about range are only available in 19 cases. These are set out in *Table VI.*

Final state

Table VII sets out the final state of the 90 patients. As some of the injuries have been sustained very recently this is a table of the disabilities and disfigurements as they seem likely, but in most cases there is little doubt as to whether complete recovery can be expected or not. The 3 cases of anosmia and 2 of the 4 with facial disfigurement are also listed under their eye disabilities, so that the 22 types of disability and disfigurement occurred in 17 patients. One of the patients with disfigurement is illustrated in *Fig.* 11.

Discussion

The purpose of this article is to give a description of the type of injuries caused by rubber bullets. While we have reported on every case attending the Royal Victoria Hospital, the Royal Belfast Hospital for Sick Children and the Altnagelvin Hospital, Derry, in the period under study, these cases are not necessarily typical of all the injuries that occurred, as emotional and other factors play a part in determining whether hospital attendance takes place or not. Some will avoid attending hospital for fear of being judged guilty of rioting. Others will attend for propaganda or litigation purposes, when they believe that it may help them to establish that they have been wrongfully assaulted. However, with serious injuries it is probably rare for patients not to attend hospital. This means that the sex distribution of hospitalized patients is probably fairly representative of all those injured, while the distribution of those attending as outpatients only, reflects more their motivation than the type and severity of the injury. Women formed 10 per cent of inpatients, 33 per cent of the total series and 51 per cent of outpatients. The injuries of the 49 outpatients should, therefore, be regarded merely as examples of a few of the minor injuries which were sustained. On the other hand, the injuries of the 41 inpatients can be looked upon as being a fairly complete list of all the severe injuries which have occurred. The age distribution shows that 64 per cent of patients were in the second decade, and most of these were between the age of 1[illegible] and 14. For inpatients and outpatients the range is similar and severe injuries occurred in all groups. The predominence of young boys is therefore most likely due to the age distribution of the population at risk on the streets, and not due to the susceptibility of their tissues to injury.

As the missile is so erratic in its flight, one would expect random injuries all over the body in proportion to the surface area of each region. The surface area of the head and neck is 9 per cent, and of the lower limbs is 36 per cent. Statistically this means that the 51 head injuries in the series should have been matched by 204 leg injuries (in our series there were only 11), and that the 33 head injury patients who were admitted should have been coupled with 132 leg injuries. In fact, no patient was admitted with a leg injury. It is obvious that the tissues of the eyes, face and skull bones and brain are particularly susceptible to a blow from a missile of this size, weight and speed. The abdomen is not nearly so susceptible as the chest. Head injuries are particularly serious as brain damage may be fatal, and a very high percentage of injuries to the eye results in blindness. While damage to thoracic and abdominal organs is comparatively rare, it would appear that injuries are possible to all the viscera.

The question of range is difficult to assess. We have been dependent on estimates by the patients or their relatives and friends. Judging distances at any time is not easy and in a highly charged emotional atmosphere one has to treat all information with a certain scepticism. However, many of these estimates were obtained within minutes of the injury and in some cases careful measurements were taken by friends. In two street situations it was possible, by examining the location of the incident, to confirm the patient's judgement.

Allowing for inaccuracies in particular estimates, it is nonetheless probable that the general picture given is not far from the truth. It is striking that the range for inpatients is no shorter than that for outpatients. In the case of the boy killed the alleged range was 2–3 m. The range was 8 m in the patient with extreme facial injury and loss of both eyes. In the point blank injury only a massive bruise resulted. Other short ranges only resulted in minor injuries while some of the severe injuries had ranges of 17–25 m. This highly irregular pattern is partly due to the precise anatomical site which the bullet strikes and partly due to the flight path of the particular missile. Other factors may be important. Ricochets off the ground and walls are common with such a missile. Despite short ranges, these rapidly dissipate the energy produced and thus decrease the severity of the injury.

There was 1 death in our series and another that we heard about. In the one from our series three factors may have contributed to the fatal outcome—the short range, his age (11 years) and an end-on impact. The other case was a young man who sustained a chest injury from a rubber bullet in Strabane. He was taken to Lifford Hospital in the Republic of Ireland, but was dead on arrival. At the inquest doubt was expressed as to whether death was due directly to the chest injury or to respiratory obstruction during the journey to hospital.

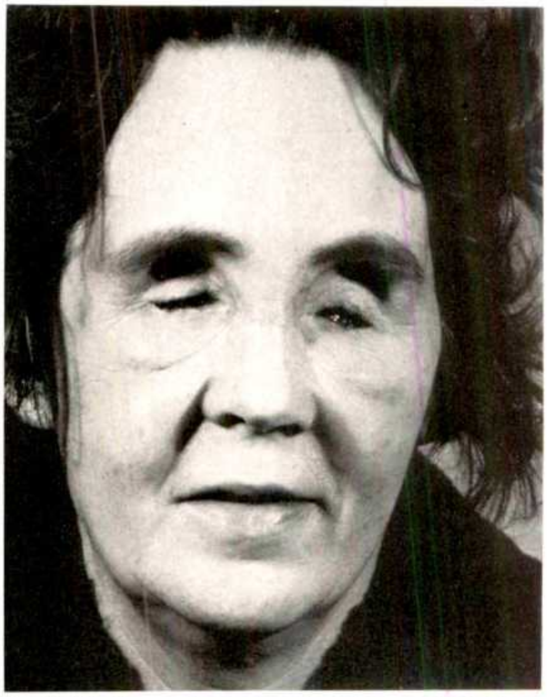


Fig. 11. Final cosmetic result in the patient shown in *Figs.* 6 and 9.

Table VI: RANGE OF BULLETS FROM FIRING TO IMPACT

Range (m)	Outpatients	Inpatients	Total
0–4	3	3	6
5–13	2	2	4
14–25	1	6	7
25	1	1	2
Total	7	12	19

Table VII: FINAL STATE

Dead	1
Blind in both eyes	2
Blind in one eye	7
Severe loss of vision in one eye	5
Disfigurement of face	4
Anosmia	3
Stiffness of finger joint	1
No permanent disability or disfigurement	62

The number of rounds fired during the period under study was approximately 33 000. With 1 death in our series and another elsewhere, this gives a mortality ratio of 1 : 16 000. Of the remaining 40 patients who required hospital admission, 17 were left with permanent disabilities or disfigurements. This gives a serious injury ratio of 1 : 800 and a disability ratio of 1 : 1900.

Despite the low mortality the rubber bullet cannot be considered completely safe in its present form. This is chiefly a consequence of its inaccuracy at the

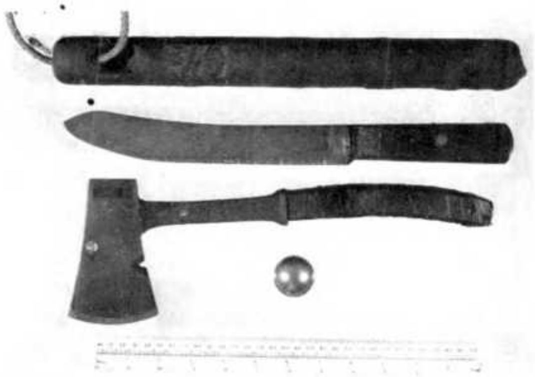


Fig. 12. Some missiles used in street riots.

recommended range of 30 or more metres. No serious injuries resulted from impacts in the lower limbs and only one from impacts on the abdomen. Impacts on the chest and head rather frequently produced serious injuries. However, not only is it impossible to avoid vulnerable areas of an individual, but the bullet may miss the target completely and strike another person. It would, therefore, be desirable to replace the present missile with one whose accuracy is considerably increased without a simultaneous increase in wounding potential. We are interested to hear that such a missile has recently been produced. It is a bullet made of solid plastic material and is said to be much more accurate.

The whole question of the use of rubber bullets cannot be fully understood without some reference to the context in which they are used. *Fig*. 12 shows some of the missiles which have been thrown in street riots in Belfast. If rubber bullets were withdrawn and the soldiers were armed only with rifles and machine guns it is certainly possible that the mortality and morbidity would have been much higher.

Acknowledgements

We are grateful to our colleagues in the hospitals of Belfast and Londonderry who supplied us with details of their cases. We thank the Medical Illustration Department of the Royal Victoria Hospital for their help, and patients and their relatives for giving permission for the use of photographs.

Reference

SHAW J. (1972) Pulmonary contusion in children due to rubber bullet injuries. *Br. Med. J.* **4**, 764–766.

Br. J. Surg. Vol. 62 (1975) 487–489

Incidental appendicectomy with laparotomy for trauma

LAWRENCE W. NORTON, MARNA SWEENEY AND BEN EISEMAN*

SUMMARY

Incidental appendicectomy was performed in 83 of 206 patients undergoing laparotomy for abdominal trauma. No organs were injured in 42 per cent of the appendicectomy patients and in 17 per cent of the non-appendicectomy patients, thus making comparison between the groups unreliable. While the incidence of intestinal perforation was 21 per cent in the appendicectomy patients, the rate of wound infection was only 7 per cent. One complication (pelvic abscess) was possibly attributable to incidental appendicectomy.

Since males below the age of 50 face a significant risk of future appendicitis and represent the majority of patients with abdominal trauma, it may be advisable to perform incidental appendicectomy with laparotomy for trauma in such patients. Specific indications for incidental appendicectomy during laparotomy for trauma are suggested.

REMOVAL of a normal appendix is an acceptable addition to many elective operations. The rationale is to eliminate the risk of future appendicitis without increasing the operative morbidity. Numerous reports indicate that incidental appendicectomy can accomplish these goals during routine hysterectomy (Beath et al., 1958), cholecystectomy (Lowery and Lenhardt, 1962) and herniorrhaphy (Brown et al., 1962).

Incidental appendicectomy during laparotomy for trauma is usually avoided, however, because of reluctance to prolong the operating time by adding unessential surgery or to risk contamination by transecting a faeces-containing organ. Since abdominal trauma often occurs in younger persons who carry a significant risk of developing appendicitis in later life, it is reasonable to consider the advisability of incidental appendicectomy at the time of laparotomy for trauma. The morbidity of such surgery has not been determined.

This is a selective preliminary study evaluating the risk of performing appendicectomy during laparotomy for trauma. It suggests that incidental appendicectomy adds little, if any, morbidity to such surgery.

Patients and methods

During the 12-month period from May 1969 to April 1970 a total of 218 patients underwent laparotomy for abdominal trauma at the Denver General Hospital. Twelve patients died during surgery or immediately thereafter and were not included in the study. The remaining 206 patients survived for 5 days or longer. Of these, 154 were males and 52 were females. Their ages ranged from 5 to 72 years with a mean age of 28 years.

The cause of injury was gunshot in 78 (38 per cent), blunt trauma in 76 (37 per cent) and stabbing in 52 (25 per cent) patients. All the patients were received in the Emergency Department within 3 hours of injury. The mean interval between injury and initial examination was 35 minutes.

Incidental appendicectomy was performed in 83 patients (37 per cent of all the patients) during the course of abdominal surgery. Operations were performed by a total of 18 different surgical residents under direct operating room supervision of a staff surgeon. Surgeons removed the appendix when the initial incision provided adequate exposure and when the patient's condition was judged to be stable. Only 2 patients were found to have a surgically absent appendix. They were included in the non-appendicectomy group. No attempt was made to randomize patient selection.

Appendicectomy technique was uniform despite the large number of surgeons. Routinely, the base of the appendix was transected between clamps, tied with absorbable suture material and inverted through a silk purse string suture. No drains or antibiotics were used specifically because of appendicectomy.

Patients with and without appendicectomy were analysed for age, sex, type and degree of injury, preoperative status, postoperative complications and survival. Follow-up ranged from 5 days to 2 years with a mean of 2 months.

Results

The average age of the 83 appendicectomy patients was 29 years compared with 27 years for the non-appendicectomy patients. Males constituted 84 per cent of the appendicectomy group and 75 per cent of the others.

Table I: MECHANISMS OF INJURY

	Appendicectomy		Non-appendicectomy	
Injury	No.	%	No.	%
Gunshot	33	40	44	36
Stab	23	27	30	24
Blunt	27	33	49	40

The mechanisms of injury are listed in *Table I*. About one-quarter of the injuries in each group were inflicted by stabbing. The incidence of blunt trauma was slightly higher in the non-appendicectomy (40 per cent) than in the appendicectomy (33 per cent) patients.

---

* Department of Surgery, Denver General Hospital and the University of Colorado School of Medicine, West 8th Avenue and Cherokee Street, Denver, Colorado, 80204, USA.

Table II: ORGAN INJURY

No. of organs injured	Appendicectomy		Non-appendicectomy	
	No.	%	No.	%
None	35	42	21	17
One	33	40	55	45
Two	9	11	37	30
Three	5	6	9	7
Four or more	1	1	1	1

Table III: MAJOR POSTOPERATIVE COMPLICATIONS

Complication	Appendicectomy	Non-appendicectomy
Sepsis	1	3
Pneumonitis	2	10
Pulmonary embolism	0	2
Stress ulcer	2	1

The interval between injury and surgery averaged slightly more than 2 hours for both groups. Twenty (23 per cent) non-appendicectomy patients were hypotensive with a systolic blood pressure of less than 80 mm Hg at some time prior to surgery. Only 6 (7 per cent) appendicectomy patients were similarly hypotensive.

The number of abdominal organs injured in each group is shown in *Table II*. Negative laparotomy with no significant organ injury was more common in appendicectomy (42 per cent) than in non-appendicectomy (17 per cent) patients. The incidence of injury to one, three and four or more organs was similar in the two groups although two organ injury was more common in the non-appendicectomy patients.

The small intestine was perforated in 14 per cent of the appendicectomy patients and in 16 per cent of the others. Large bowel perforation occurred in 7 and 8 per cent respectively. In no case was the appendix itself injured. The incidence of splenic injury was comparable but liver injury was proportionately more common in the non-appendicectomy patients.

Wound infection, defined as purulent wound drainage with or without micro-organisms, occurred in 6 (7 per cent) appendicectomy and 21 (17 per cent) non-appendicectomy patients. Gram-negative bacteria were recovered from 7 of the latter wounds and from only 1 of the former. Staphylococci were cultured from half of the infected wounds in both groups.

Postoperative complications other than wound infection included sepsis, pulmonary embolism, pneumonia and stress ulcer (*Table III*). The incidence of complications was considerably higher in non-appendicectomy (32 per cent) than in appendicectomy (14 per cent) patients. With one exception, no significant sepsis occurred in the patients with incidental appendicectomy.

The single complication possibly attributable to appendicectomy was in a 19-year-old male with rupture of the spleen secondary to blunt abdominal trauma. Ten days after splenectomy and appendicectomy a pelvic abscess was drained. No bacteria were cultured from the abscess pus. The site of the appendicectomy appeared to be healing normally.

No operative deaths occurred among the patients with appendicectomy. Eight (6·5 per [illegible] non-appendicectomy patients died 5–25 days af[illegible] surgery. Respiratory complications were responsi[illegible] half of these deaths.

Discussion

Incidental appendicectomy can be justified only if the risk of future appendicitis exceeds the risk of complications resulting from the appendicectomy. Several recent studies indicate that the risk of appendicitis is significant under the age of 50 (Ludbrook and Spears, 1965; Ashley, 1967; Hewitt et al., 1969). Hewitt et al. (1969) determined that in early childhood almost 1 person in 6 can expect to undergo primary appendicectomy for suspected appendicitis. After the age of 50 the risk is 1 in 40. The expectation of appendicitis in a person 28 years old (the mean age of our injured patients) is about 1 in 18.

Until the age of 50, males have a slightly greater expectation of undergoing primary appendicectomy than females. At the age of 28, for instance, the probability of a male developing appendicitis in the next year of life is about 15 per cent greater than that of a female. In both males and females the risk of death from appendicitis is about 1 in 800.

It appears that the younger male, who is most apt to undergo laparotomy for trauma, faces an appreciable risk of developing appendicitis at some time in the future, although his expectation of death from such disease is negligible.

Numerous authors have evaluated the risk of incidental appendicectomy with elective operations (Howie, 1968). Myers and Schreier (1960) found no greater incidence of postoperative morbidity among 483 obstetrical surgery patients with incidental appendicectomy than among 1201 similar patients without appendicectomy. This experience has been confirmed in obstetrical and gynaecological procedures by Beath et al. (1958). Incidental appendicectomy has been reported to be possible during vaginal surgery without increasing the incidence of complications (McGowan, 1968).

Eiseman et al. (1959) found that appendicectomy performed during right inguinal herniorrhaphy in 429 patients increased neither recurrence nor complication rates. Keeley and Schairer (1962) and Shumake (1971) have reported a similar experience.

Whether incidental appendicectomy is as innocuous during cholecystectomy is debated. Komorn and Kaufman (1963), reporting 62 cases, found a wound infection rate nearly three times higher than in non-appendicectomy cholecystectomy patients. Conversely, Lowery and Lenhardt (1962) and Bogart and Sebesta (1969) reported no increase in complications when the appendix is removed during cholecystectomy. Interestingly, Lowery and Lenhardt (1962) found that 28 per cent of incidentally removed appendices were abnormal histologically. This appears to be a unique experience unsubstantiated in our patients or in other series.

Obviously the two groups of patients reported here are not comparable. The degree of injury in the non-appendicectomy patients as a whole was greater as evidenced by a higher incidence of preoperative hypotension, postoperative complications and deaths. No serious visceral injury was found in 42 per cent of the appendicectomy patients and in only 17 per cent of the non-appendicectomy group. Thus, many of the appendicectomies were simply a byproduct of negative laparotomy. This intrinsic selection prevents accurate comparison of morbidity and mortality between appendicectomy and non-appendicectomy patients.

It is significant, however, that with perforation of the intestine in nearly one-quarter (21 per cent) of the appendicectomy patients, the rate of wound infection was only 7 per cent, a figure comparable to that after elective uncontaminated operations.

Only one possible complication of incidental appendicectomy was identified. It is unlikely that pelvic abscess in a patient with splenic rupture would have occurred without appendicectomy, although evidence of definite faecal contamination was absent.

This preliminary study suggests that incidental appendicectomy does not appreciably increase the morbidity of laparotomy for trauma. A randomized, prospective trial is required to confirm this impression. Current evidence also suggests that incidental appendicectomy with laparotomy for trauma may be particularly advisable in the male under 50 years of age.

The precise circumstances in which it is justified to perform appendicectomy during laparotomy for trauma remain to be defined. All justification obviously assumes that the satisfactory condition of the patient will not be compromised by the slight additional operative time and theoretical threat of contamination. At the time of laparotomy for trauma incidental appendicectomy should be considered with progressively less enthusiasm under the following conditions:

1. *Negative exploration*: If laparotomy shows no visceral injury, appendicectomy is advisable and should entail no greater risk than with an elective operation.
2. *Perforating wounds of the small or large bowel*: When the peritoneal cavity is already grossly soiled with intestinal contents, appendicectomy cannot appreciably add to the hazard of infection.
3. *Perforating wounds of the stomach*: Since gastric contents are usually sterile and perforating wounds of the stomach heal well, the addition of incidental appendicectomy to repair of minor gastric perforations seems reasonable. It is analogous to adding appendicectomy to elective gastric surgery for ulcer disease.
4. *Splenic injury*: Splenectomy for injury characteristically involves little risk of sepsis. Adding appendicectomy to splenectomy should be nearly the equivalent of performing appendicectomy at a negative laparotomy, assuming that all the blood is evacuated from the peritoneal cavity.
5. *Major vascular repair*: If there are no other damaged organs and injury to a major vessel such as the abdominal aorta or vena cava can be repaired by suture alone, appendicectomy should not add a significant risk. It should not be employed where a prosthesis is required.
6. *Hepatic and pancreatic injury*: Bile, blood, pancreatic juice and bacteria comprise such a dangerous pabulum that only with the most minor damage to the liver and pancreas should incidental appendicectomy be performed.

Even these relative indications for appendicectomy must be ignored if the patient's general condition is unstable or the appendix cannot be visualized in its entirety without extensive dissection.

References

ASHLEY D. J. B. (1967) Observations on the epidemiology of appendicitis. *Gut* **8**, 533–538.

BEATH D. H., HOLMES D. E., NOEL P. J., POWELL D. V. and YARD G. H. (1958) Incidental appendectomy in obstetrics and gynecology. *Obstet. Gynecol.* **12**, 727–732.

BOGART J. N. and SEBESTA D. G. (1969) Incidental appendectomy and its effect on the incidence of wound infection in cholecystectomy. *Am. Surg.* **35**, 650–652.

BROWN J. B., EISEMAN B. and ROBINSON R. M. (1962) simultaneous appendectomy and herniorrhaphy without prophylactic antibiotic therapy. *Surgery* **51**, 578–582.

HEWITT D., LE RICHE W. H. and MILNER J. (1969) Incidental appendectomy: a statistical appraisal. *Can. Med. Assoc. J.* **100**, 1075–1081.

HOWIE J. G. R. (1968) The morbidity of appendicectomy *Scott. Med. J.* **13**, 72–77.

KEELEY J. L. and SCHAIRER A. E. (1962) Incidental appendectomy during repair of groin hernias. *Surgery* **52**, 421–423.,

KOMORN H. and KAUFMAN L. W. (1963) Incidental appendectomy during gall bladder surgery. *Sinai Hosp. Detroit Bull.* **11**, 103–106.

LOWERY C. H. and LENHARDT H. F. (1962) Incidental appendectomy during gall bladder surgery. *Arch. Surg.* **85**, 476–479.

LUDBROOK J. and SPEARS G. F. S. (1965) The risk of developing appendicitis. *Br. J. Surg.* **52**, 856–858.

MCGOWAN L. (1968) Incidental appendectomy during vaginal surgery. *Am. J. Obstet. Gynecol.* **95**, 588.

MYERS J. D. and SCHREIER P. C. (1960) Appendectomy incidental to caesarean section, postpartum sterilization, or ectopic pregnancy. *South. Med. J.* **53**, 359–361.

SHUMAKE L. B. (1971) Right inguinal herniorrhaphy and incidental appendectomy. *Am. Surg.* **37**, 310–311.

Br. J. Surg. Vol. 62 (1975) 490–494

A prospective study of acute pancreatitis

C. W. IMRIE AND A. S. WHYTE*

SUMMARY

All 78 patients with acute pancreatitis admitted to one hospital in a 2-year period were included in a prospective survey of conservative management. The overall mortality rate was 11·5 per cent, being 46 per cent for 11 patients subjected to early laparotomy and only 6 per cent for patients managed without operation. Twenty-six patients were considered to have severe acute pancreatitis and all 9 deaths occurred in this group.

Biliary disease was present in 51 per cent of patients, and the majority of those with biliary disease were over 60 years old. Alcohol-related acute pancreatitis occurred in 26 per cent of the total patients, and none of this group was over 60 years old. Acute pancreatitis was considered idiopathic in origin in only 13 per cent of the patients.

Elective biliary surgery in 30 patients has resulted in freedom from recurrent attacks of acute pancreatitis for the follow-up period (12–30 months).

The results compare favourably with those in which glucagon and high dosage aprotinin (Trasylol) have been utilized in the management of acute pancreatitis.

THE mortality rate for acute pancreatitis in the United Kingdom has been reported as 20–25 per cent (Pollock, 1959; Trapnell, 1966). Recent studies have indicated that certain specific therapeutic agents may be of value in the management of acute pancreatitis. Thus, intravenous glucagon was utilized in an uncontrolled study of the management of 30 patients (Condon et al., 1973). There were only 2 deaths in this group and it was proposed that glucagon may be of value in reducing the mortality rate. By contrast, a controlled double blind trial of high dosage aprotinin (Trasylol) revealed a difference between a control group of 52 patients, in which the mortality rate was 25 per cent, and the Trasylol-treated group of 53 patients with a mortality rate of 7·5 per cent (Trapnell et al., 1974).

The present article reports the results of the initial 2 years of a prospective survey of acute pancreatitis. A well-supervised conservative management regimen was utilized and neither glucagon nor Trasylol was administered.

Patients

All 78 patients with acute pancreatitis admitted to Glasgow Royal Infirmary in 1971 and 1972 were included in the study. The surviving patients have been followed up on a regular basis as outpatients and 94 per cent have been seen at least 1 year after their initial attack. Clinical examination, haematological and biochemical estimations including liver function tests and estimations of fasting cholesterol and triglyceride levels together with biliary radiology were performed in all the cases.

Diagnostic criteria

The diagnosis was based on the clinical presentation, hospital course of the illness and biochemical findings in 67 patients, while the diagnosis was not suspected and thus made at laparotomy in 11 patients. Over 90 per cent of the patients presented with upper abdominal pain, and only 2 of the 78 cases had no vomiting recorded. Only 6 patients had previously suffered an attack of acute pancreatitis. Serum amylase elevations greater than 1200 i.u./litre were accepted as confirming the initial diagnosis.

The majority of patients had timed urine collections performed which allowed calculation of amylase clearance and creatinine clearance. The normal range of amylase clearance is 2·7–3·1 ml/min and in acute pancreatitis usually exceeds 4 ml/min (Levitt et al., 1969). A high amylase clearance was useful in confirming the diagnosis in 13 patients presenting later than 24–48 hours after the onset of symptoms, and defined a single case of macro-amylasaemia with characteristic low amylase clearance (Imrie et al., 1973).

The criteria for accepting biliary disease as an aetiological factor were operative and histological. Radiological evidence was accepted on its own in 5 patients only, who were unwilling or unfit for surgery.

On admission to hospital all the patients were specifically questioned and an assessment made of alcohol intake. Patients accepted as having a regular heavy intake of alcohol consumed on a daily basis at least 350–700 ml of whisky or 3 litres of beer or 500 ml of wine.

Acute renal failure was accepted when a rise in blood urea over 100 mg/100 ml failed to respond to adequate fluid replacement.

Assessment of severity

It is difficult to assess accurately the severity of an attack during the early period of admission to hospital. Initial severe hypotension and hypovolaemia often respond rapidly to fluid replacement. Many of the best indices of severity are only apparent after a longer stay in hospital. The severity of the attack was assessed in retrospect based on the following criteria: (1) hypocalcaemia (< 8·0 mg/100 ml), (2) acute renal failure and (3) pseudocyst or abscess formation (Trapnell 1966, 1971).

---

* Glasgow Royal Infirmary.

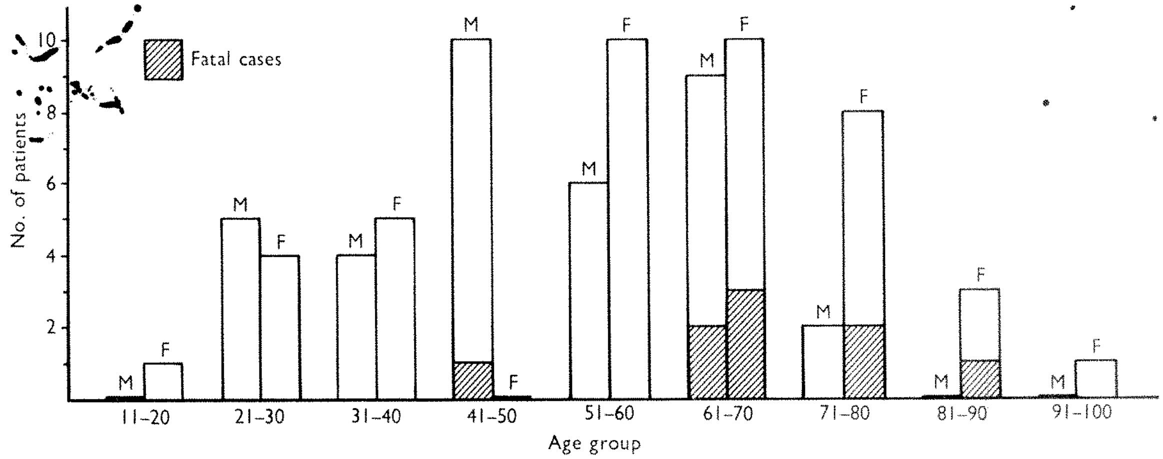


Fig. 1. Age and mortality of patients with acute pancreatitis.

Management

Each patient was seen at least daily by one of us. Management was by nasogastric suction and the administration of intravenous fluids. Pethidine (50–150 mg according to body weight) was the analgesic routinely used. Antibiotics and anticholinergics were not administered routinely.

Intravenous fluid replacement was based on normal saline, Ringer's lactate and dextrose solutions with the necessary addition of potassium and calcium supplements. Dextran solutions, plasma and blood were given on specific indications. Parenteral intravenous amino-acid and lipid solutions to provide calories were reserved for patients who required intravenous therapy for longer than 1 week.

If any doubt existed as to satisfactory urinary output, catheterization was carried out and hourly urine volumes monitored with the aim of maintaining a minimum level of output of 30 ml/hour. To achieve this, a high rate of intravenous infusion was frequently required. Central venous pressure was recorded during such infusion. Failure to ensure adequate urinary output was then treated by the intravenous administration of mannitol or frusemide.

Results

There were 36 male and 42 female patients in the study and 9 died (11·5 per cent mortality). All 9 deaths occurred in a group of 26 patients who met the criteria for severe disease. Only 6 per cent of those managed conservatively died, and 19 of this group of 67 patients were considered to have severe disease.

The younger patients (< 60 years old) had a much better prognosis than did the older patients (*Fig.* 1, *Table I*). A high incidence of biliary disease occurred in young females (*Table II*), while in young males a high incidence of alcohol-related pancreatitis was found (*Table III*). The only fatal case in this age group was a 41-year-old male with alcohol-related pancreatitis.

Patients over the age of 60 had a much higher mortality rate (*Fig.* 1, *Table I*), and in contrast to the young patients none was considered to have alcohol-related acute pancreatitis.

Table I: AGE AND MORTALITY IN ACUTE PANCREATITIS

Age	Male	Female	Mortality No.	Mortality %
Up to 60 years	25	20	1	2·2
Over 60 years	11	22	8	24·2
Total	36	42	9	11·5

Table II: INCIDENCE OF BILIARY DISEASE ACCORDING TO AGE AND SEX

Age	Male No.	Male %	Female No.	Female %
Up to 60 years	3	12	16	80
Over 60 years	7	64	14	64

Percentage figures refer to proportion of biliary disease cases in each subgroup.

Table III: INCIDENCE OF ALCOHOL-RELATED PANCREATITIS ACCORDING TO AGE AND SEX

Age	Male	Female
Up to 60 years	19	1
Over 60 years	0	0

Associated aetiological factors

The importance of identifying aetiological factors in acute pancreatitis has frequently been stressed because elimination of such factors may protect the individual patient from recurrent attacks.

Biliary disease

Forty patients (51 per cent of the total) had biliary disease (*Table IV*) and the mortality rate of this group was 12·5 per cent. Twelve were shown to have a common bile duct disorder, either stones or debris. The incidence of biliary disease is greatest in younger female patients, and for older patients the incidence for each sex is identical (*Table II*).

The results of elective surgery for biliary tract disease are shown in *Table V*. In the patient who had

Table IV: SUMMARY OF ASSOCIATED FACTORS

Associated factor	No. of cases	% of total
Biliary disease	40	51
Alcohol	20	26
Recent surgical operation	4	5
Pregnancy/puerperium	3	4
Blind loop	3	4
Duodenal ulcer	3	4
Pancreatic carcinoma	2	3
Hypothermia	2	3
Idiopathic	10	13

Table V: EFFECT OF ELECTIVE BILIARY SURGERY ON RECURRENCE

	No.	Recurrence
Elective surgery	30	1*
No elective surgery	5	2
Fatal cases	5	—

* *See* text.

Table VI: MORTALITY IN RELATION TO OPERATIVE AND NON-OPERATIVE MANAGEMENT IN EARLY PHASE OF TREATMENT

		Mortality	
Treatment	Total	No.	%
Operative	11	5	45·5
Non-operative	67	4	6·0
Total	78	9	11·5

a postoperative recurrence, retained stones within the common bile duct were demonstrated on endoscopic retrocholedochopancreatography (Blumgart et al., 1972). Removal of these at a further operation has resulted in a symptom-free period of over 18 months. By contrast 5 of the patients not operated on electively died, and 2 of the survivors have suffered recurrent attacks of acute pancreatitis. One patient has been lost to follow-up and the remaining 2 are well.

Three of the 5 fatal cases had surgery performed while suffering from acute pancreatitis. Two had a laparotomy performed within 24 hours of hospital admission because of diagnostic uncertainty, and the third had cholecystectomy and common bile duct exploration performed 22 days after the onset of a prolonged attack of pancreatitis in an attempt to improve the course of the disease.

Alcohol

Twenty patients, all less than 60 years old, suffered acute pancreatitis within 36 hours of heavy alcohol intake. Only 1 patient in this group died. However, the recurrence rate was very high and of the 17 cases reviewed at follow-up, only 2 have been free from further attacks. Both have abstained from alcohol.

Other associated factors

Three patients experienced their first attack of acute pancreatitis within 3 months of parturition, but biliary disease was present in all 3.

It is of interest to note that there were 3 patients who had both a gastro-enterostomy and biliary disease. Another 3 were known to have coincidental duodenal ulceration and 1 of these was treated surgically at the same operation as elective cholecystectomy and exploration of the common bile duct. Pancreatic carcinoma was diagnosed in 2 patients who originally presented with clinical and biochemical evidence of acute pancreatitis. Finally, severe hypothermia (rectal temperature 29 °C) was present in 2 female patients on admission.

Idiopathic cases

There were 10 instances in whom an associated aetiological factor could not be defined. In this group 5 elderly patients were considered on radiological and clinical grounds to have probable, but not proved, biliary disease. No case of hyperparathyroidism or hyperlipoproteinaemia was identified. Acute and convalescent viral titres were estimated in several of this idiopathic group, and no elevated values recorded.

Postoperative pancreatitis

Four patients developed postoperative pancreatitis. Three, of whom 2 had been subjected to transduodenal sphincterotomy, were diagnosed in the immediate postoperative period. The third patient had a retained stone present after choledochotomy. All 3 had large volumes of postoperative nasogastric aspirate or vomiting, and in 2 severe upper abdominal pain was also present. Grossly elevated serum and urine amylase levels were found in all 3.

The fourth patient developed acute pancreatitis 7 days after surgery unrelated to the biliary tract. All of these patients survived.

Effect of early surgical intervention (*Table VI*)

Eleven patients had a laparotomy performed within 24 hours of emergency hospital admission because of uncertainty of diagnosis. Laparotomy was performed with or without tube drainage and only 1 of these patients had the additional prodecure of cholecystostomy performed. Five died (mortality 46 per cent). The period from diagnosis to death varied from 2 to 55 days, and additional factors contributing to death were present in most cases (*Table VII*). Similarly, in the 4 fatal instances within the group of patients managed conservatively additional factors were present and the deaths occurred from 10 to 70 days after admission (*Table VIII*).

Calcium and phosphate changes

Serum calcium levels examined retrospectively were found to have been associated with a poor prognosis, there being 7 deaths in 15 patients with calcium levels of less than 8·0 mg/100 ml. It was also noted that serum phosphate levels frequently fell below 2·0 mg/100 ml (14 patients), although only 5 patients had simultaneous falls in the calcium level below 8·0 mg/100 ml. Hypophosphataemia was transient and occurred on the second to fourth day after admission to hospital.

Transaminase elevations

Significant rises in serum transaminase levels occurred in 20 of the 67 cases in which they were measured. Elevations of transaminases were in most cases of a temporary nature, running a course parallel to the elevations of serum amylase. In every case one or both enzyme levels exceeded the upper limit of normal by at least a factor of 2·5. In only 12 of these 20 cases did bilirubin levels exceed normal values, but 17 of the 20 showed accompanying elevations in alkaline phosphatase.

Complications

Table IX lists the complications and their relation to the outcome. The adverse prognostic association of acute renal failure and gastro-intestinal bleeding (Trapnell, 1971) is clear.

Discussion

This study has demonstrated that good conservative management without the addition of specific drugs can be associated with a mortality rate of less than 12 per cent in acute pancreatitis. If operation is avoided, then this mortality can be reduced to 6 per cent. A further 62 patients have been studied during 1973 and confirm these views, the overall mortality for all the patients being 10 per cent. Even if patients with alcohol-related disease are excluded, then the mortality rate is 11 per cent and comparable to that recorded for high dosage trasylol treatment (Trapnell et al., 1974).

Factors which may have contributed to this reduced mortality are a low incidence of diagnosis by laparotomy in comparison with retrospective studies (Trapnell and Anderson, 1967; Imrie, 1974), early diagnosis because of clinical awareness, better methods of accurately measuring serum and urinary amylase concentration, an appreciation of risk from operations on the biliary tree and the personal care which comes from concentration on a problem. However, there remains room for further improvement in that in all the 11 instances of diagnosis at laparotomy the disorder had not been considered and amylase levels not ascertained. Before proceeding to laparotomy—which in our experience was associated with the death of nearly half those submitted to it—not only should amylase levels be determined but also consideration given to peritoneal aspiration through a dialysis catheter (Elliott, 1971). We have recently used this and determined the amylase and bacterial contents of the aspirate before a final decision on laparotomy.

Why patients die after laparotomy is not clear, but hypoxia may be important. Twenty-five of 34 of our patients in whom blood gas analysis was done within 24 hours of admission but before surgery had arterial P_{O_2} levels of less than 70 mm Hg, a finding already recorded by others (Ranson et al., 1973). Surgical exploration will only make such a disturbance worse.

A further lethal event in past series has been acute renal failure and although our incidence is low, our experience of the developed condition remains unsatisfactory with 4 out of 5 patients failing to survive. The wider use of peritoneal dialysis (Gliedman et al., 1970) may alter this gloomy outlook and we have recently successfully managed the pancreatitis and renal insufficiency of 2 patients in this way.

Table VII: SUMMARY OF THE PATIENTS WHO DIED OF ACUTE PANCREATITIS AFTER UNDERGOING LAPAROTOMY

Sex	Age	Major factors	Time of death (days from onset)
M	41	ARF; bacteraemic shock	9
M	69	Perforation of colon; faecal peritonitis	55
M	70	ARF; lung abscesses; severe diabetes; DVT + PTE	26
F	79	ARF; cerebrovascular accident	31
F	86	None known	2
Mean age 69			Mean 24·6

ARF, Acute renal failure. DVT, Deep vein thrombosis. PTE, Pulmonary embolism.

Table VIII: SUMMARY OF THE PATIENTS WHO DIED OF ACUTE PANCREATITIS WHICH WAS TREATED CONSERVATIVELY

Sex	Age	Major factors	Time of death (days from onset)
F	62	None known	28
F	65	Pleural effusion; diffuse haemolysis	70
F	66	ARF; lung abscess; gross hypothermia; CCF	12
F	79	Bacteraemic shock	10
Mean age 68			Mean 30

ARF, Acute renal failure. CCF, Congestive cardiac failure.

Table IX: COMPLICATIONS OF ACUTE PANCREATITIS

Complication	No. of cases	% of total	No. of deaths
Acute renal failure	5	6	4
Pseudocyst	4	5	—
Diabetes	4	5	1
Pancreatic abscess	3	4	—
Gastro-intestinal bleeding	3	4	2
Wound dehiscence	3	4	—
Postoperative fistula	2	3	—
Pleural effusion	2	3	1

No previous British survey of acute pancreatitis has revealed such a high incidence of alcohol-related cases, although a similar incidence was reported from Edinburgh hospitals (Gillespie, 1973). An overall increase in alcohol intake is reflected in a 12 per cent incidence of alcohol-related acute pancreatitis in England (Trapnell, 1972), and an increased incidence of alcohol-related chronic pancreatitis (James et al., 1974).

A high proportion of alcohol-related cases in any particular group studied may contribute to a lower mortality (Gliedman et al., 1970). However, it is noteworthy that in the present study none of the patients with alcohol-related pancreatitis was over 60 years old, while 53 per cent of the patients with biliary disease were over this age. It is therefore possible that the different age groups of the patients, rather than the different aetiological factors, may be of greater importance in determining the mortality rate for these two groups. Because of our ability to relate the disease to causes such as alcohol, we have only a few idiopathic cases, in contrast to others (Sarles et al., 1965; Trapnell, 1966). We have confirmed that elective biliary surgery will prevent recurrence of pancreatitis, and that careful exploration of the common duct yields a 30 per cent incidence of stones and debris.

Evaluation of laboratory results has revealed two other matters which have received little previous attention in addition to the well-known relationship between hypocalcaemia and poor outlook. First, a quarter of our patients had elevated transaminase levels, as did those of one other series (Lukash, 1967), and only two-thirds of these had synchronous rises in bilirubin concentration. Secondly, the profound fall in phosphate levels has not previously been recorded. The most severe degrees of hypocalcaemia were not invariably linked to these changes in phosphate levels, but nevertheless falls in the level of ionic calcium may be the stimulus to increased parathormone release resulting in phosphaturia. This hypothesis must await reliable assays for parathormone in addition to measurements of ionic calcium levels in these patients.

In conclusion, it is clear that there are no obvious differences between the mortality rate of primary acute pancreatitis managed conservatively as in this study and the published results of management which includes high dosage treatment with Trasylol or glucagon.

Acknowledgements

We thank the consultants of the surgical and medical divisions of Glasgow Royal Infirmary for their cooperation and permission to study cases under their care. Particular thanks are due to Professor L. H. Blumgart for his help and constructive criticism during the preparation of this paper. A study of this type would be impossible without the great assistance of the nursing staff in collecting the essential urine specimens and of the many housemen who helped in taking blood specimens. We thank these members of staff and also those of the Biochemistry Department for invaluable help.

References

BLUMGART L. H., COTTON P. B., BURWOOD R., LAWRIE B., SALMON P., DAVIES G. T., BEALES J. S. M., SKIRVING A. and READ A. E. (1972) Endoscopy and retrograde choledochopancreatography in the diagnosis of the jaundiced patient. *Lancet* **2**, 1269–1273.

CONDON J. R., KNIGHT M. and DAY J. L. (1973) Glucagon therapy in acute pancreatitis. *Br. J. Surg.* **60**, 509–511.

ELLIOTT D. W. (1971) In: IRVINE W. T. (ed.) *Recent Advances in Surgery*. London, Butterworths. pp. 136–150.

GILLESPIE W. J. (1973) Observations on acute pancreatitis, a retrospective clinical study. *Br. J. Surg.* **60**, 63–65.

GLIEDMAN M. L., BOLOOKI H. and ROSEN R. G. (1970) *Acute Pancreatitis*. (*Current Problems in Surgery*.) Chicago, Year Book.

IMRIE C. W. (1974) Observations on acute pancreatitis. *Br. J. Surg.* **61**, 539–544.

IMRIE C. W., KING I. and HENDERSON A. R. (1973) Macroamylasaemia: a report of 2 cases. *Scott. Med. J.* **18**, 188–191.

JAMES O., AGNEW J. E. and BOUCHIER J. A. D. (1974) Chronic pancreatitis: a changing picture? *Br. Med. J.* **2**, 34–39.

LEVITT M. D., RAPOPORT M. and COOPERBAND S. R. (1969) The renal clearance of amylase in renal insufficiency, acute pancreatitis and macroamylasaemia. *Ann. Intern. Med.* **71**, 919–925.

LUKASH W. M. (1967) Complications of acute pancreatitis, unusual sequelae in 100 cases. *Arch. Surg.* **94**, 848–852.

POLLOCK A. V. (1959) Acute pancreatitis, analysis of 100 patients. *Br. Med. J.* **1**, 6–14.

RANSON J. H. C., ROSES D. F. and FINK S. D. (1973) Early respiratory insufficiency in acute pancreatitis. *Ann. Surg.* **178**, 75–79.

SARLES H., SARLES J. C., CAMATTE R., MURATORE R., GAINI M., GUIEN C., PASTOR J. and LE ROY F. (1965) Observations on 205 confirmed cases of acute pancreatitis, recurring pancreatitis and chronic pancreatitis. *Gut* **6**, 545–559.

TRAPNELL J. E. (1966) The natural history and prognosis of acute pancreatitis. *Ann. R. Coll. Surg.* **38**, 265–287.

TRAPNELL J. E. (1971) Management of the complications of acute pancreatitis. *Ann. R. Coll. Surg.* **49**, 361–372.

TRAPNELL J. E. (1972) The natural history and management of acute pancreatitis. *Clin. Gastroenterol.* **1**, 147–166.

TRAPNELL J. E. and ANDERSON M. C. (1967) Role of early laparotomy in acute pancreatitis. *Ann. Surg.* **165**, 49–55.

TRAPNELL J. E., RIGBY C. C., TALBOT C. H. and DUNCAN E. H. L. (1974) A controlled trial of Trasylol in the treatment of acute pancreatitis. *Br. J. Surg.* **61**, 177–182.

Br. J. Surg. Vol. 62 (1975) 495–496

The use of the vas deferens in inguinal herniorrhaphy

PATRICK SAMES*

SUMMARY

A new method of repair of inguinal herniae is described using the vas deferens as a suture material. It is especially suitable in very large and recurrent herniae. Nineteen cases have been operated on in this way with an average of 38 months' follow-up. In none has recurrence been noted. It is suggested that the vas deferens, so readily to hand, forms a more natural barrier than man-made fibres. It may also, in fact, remain viable, though this has not, as yet, been proved.

THE surgical repair of very large and recurrent inguinal and inguinoscrotal herniae still presents a considerable problem. In the past a variety of suture materials has been used with differing results. These materials fall mainly into two groups; some form of man-made fibre, and those occurring naturally and being an integral part of the body. Darning with such substances as floss silk (Maingot, 1941) or the insertion of woven barriers of wire (McGavin, 1909) or twisted silk (Handley, 1918) has had its advocates. However, a common failing with these is the high incidence of sepsis and sinus formation, sometimes quite late in the postoperative period and occasionally necessitating a most difficult operation for the removal of the foreign substance. The advent of monofilament nylon (Moloney, 1948) considerably improved the outlook, as this substance is less likely to give rise to postoperative sinus formation, unlike its woven and multifilament counterpart. At present some form of darning operation using monofilament nylon is probably the most widely practised procedure.

The most popular operation making use of naturally occurring material is that described by Gallie and LeMesurier (1921) whereby strips of fascia lata are taken from the thigh. These are usually obtained by the use of a fasciatome but leaves the patient with an unfortunate herniation of thigh muscle through the fascial defect. Although this does not materially affect function, it is cosmetically undesirable; it has, in fact, been the basis of litigation against the surgeon. This herniation can, of course, be avoided by taking the fascia by open operation and resuturing the defect, but this then becomes a major procedure in itself. Attempts have been made to use strips of the external oblique aponeurosis at the site of the operation (McArther, 1904), but this structure is often very poorly developed in large or recurrent herniae. Free strips of skin from the edges of the incision have also been used (Mair, 1945), but have the disadvantage that inclusion dermoid or sebaceous cysts have occurred later in the depth of the wound.

Another and hitherto unexplored source of naturally occurring material available for the repair of herniae is the vas deferens, as suggested by the author in a previous communication (Sames, 1968). This structure has the advantage of being readily to hand, and is already fixed at its proximal end. The whipcord-like structure has a greater diameter than nylon and therefore fills in the fascial and muscle defects with greater certainty. In the elderly with very large and difficult herniae the testis and cord may be sacrificed, provided always that the patient has given his consent. Even when the testis is preserved, the patient's consent should be obtained as for vasectomy. This step is even more cogent should it be contemplated that bilateral herniae are to be repaired in this manner.

Technique

After the sac has been freed and dealt with in the usual manner, the vas deferens is traced down to the lower pole of the epididymis and divided at the point where it starts to become tortuous. The average length measured from high in the internal inguinal ring to the point of section is 26 cm (*Table I*). There is a marked variation in the diameter of the vas, which tends to be thinner in older subjects, although the reverse is sometimes the case. No attempt is made to clean off the flimsy integument from the vas as it is possible that the fine vessels on the outer aspect of the wall may stay intact and the vas remain viable. Unfortunately the author has not had the opportunity to confirm this by autopsy examination. In a very large direct hernia the bulging of fat and peritoneum can usually be controlled by suturing what is left of the transversalis fascia with interrupted cotton sutures. When this is not practical the use of a damp swab and narrow-bladed depressor should suffice.

When using the vas, in contradistinction to nylon darning, the repair commences at the outer end of the canal because the vas is already fixed here within the pelvis. In large saddle-backed herniae it is wise to divide the deep epigastric vessels between ligatures. The vas is too fat to thread even on to a Gallie's fascial needle, therefore suturing is carried out by pushing a Cleveland ligature carrier or fine-pointed mosquito forceps through the relevant structures, grasping the divided end of the vas and drawing it through. At the commencement the vas is brought out of the pelvis by piercing the internal oblique muscle just lateral to the ring, and then proceeding medially to fill in the gap between the inguinal ligament below

---

* Royal United Hospital, Bath.

Table I: SUMMARY OF THE PRESENT SERIES

Case	Age	Length of vas (cm)	Orchidectomy	Follow-up (mth)	Additional features
1	74	17	No	32	16 Years' duration. No truss
2	54	35	Yes	18	Apronectomy, 4·1 kg, and omental excision, 3 kg
3	43	25	Yes	40	
4	71	22	Yes	50	Large hydrocele on opposite side dealt with
5	68	22	No	52	Large direct hernia on right side
		19	No		Large sliding indirect hernia on left side
6	75	26	Yes	56	
7	46	26	No	48	
8	48	25	No	50	Postoperative deep vein thrombosis and pulmonary embolism—survival
9	76	30	Yes	58	Excision of small bowel for obstruction
10	65	28	Yes	38	
11	66	29	No	48	Saddle-back hernia. Division of deep epigastric vessels
12	75	25	No	50	
13	65	25	No	36	
14	71	21	No	14	
15	81	32	Yes	38	Large amount of omentum excised
16	51	30	No	49	Large recurrent hernia
17	56	35	No	39	
18	76	28	Yes	12	Associated large hydrocele

and the conjoint muscle and tendon above. Great care should be taken to continue the repair far into the medial angle, to the region of the pubic tubercle below and the fascial sheath of the pyramidalis or rectus muscle above.

In very large and long-standing inguinoscrotal herniae there is usually marked hypertrophy of the integument of the cord, especially the cremasteric muscle. A decision must therefore be made whether or not to include this structure in the repair. When it is to be preserved it must be trimmed to give a 'skirt' both above at the lower border of the conjoined muscle and below at the lower border of the inguinal ligaments before including it in the buttress repair. In some subjects these fasciae are only an embarrassment and as such are best sacrificed. It is vital in all cases that such clearance be made at the innermost angle in order to define properly the medial end of the inguinal ligament, the fascia over the rectus or pyramidalis muscle and the pubis tubercle. There are often numerous veins in the floor of the canal going to the scrotal skin (veins of Tasker); these should be carefully cleaned away.

When the darn is completed the free end of the vas is fixed with an interrupted cotton suture. There is usually a surplus of 2–5 cm remaining. This is then woven back on itself, passing under one strand and over the next until finally used up. The end is securely anchored with another interrupted suture. Care must be taken, when suturing down to the inguinal ligament, to pierce it at slightly different levels to avoid splitting the strands. The repair should be strictly a loose darn and no effort should be used to draw the tissues together. The external oblique aponeurosis is either repaired over or behind the cord according to local circumstances and the particular practice of the surgeon. It is wise, especially in moist cases, to drain the depth of the wound or scrotum with a Redivac suction drain.

Results

These are as shown in *Table I*. Nineteen patients have been followed up for an average of 3½ years and in none has recurrence been noted; no patient has been lost to follow-up. Wound infection occurred in 1 case, but this presented in a man who while waiting for his operation, and on a strict dieting régime, had developed signs of strangulation. He was, in fact, a mild diabetic, standing only 1·6 m high and weighing 140 kg. The repair was associated with an excision of his dewlap weighing 4 kg and of omentum weighing 3 kg. The sepsis was confined to the opposite side from his hernial repair and was no doubt associated with the moist intertrigo noted before the operation.

References

GALLIE W. E. and LEMESURIER A. B. (1924) The transplantation of fibrous tissues in the repair of anatomical defects. *Br. J. Surg.* **12**, 289–321.

HANDLEY W. SAMPSON (1918) A method for the radical cure of inguinal hernia (darn and stay-lace method). *Practitioner* **100**, 466.

MCARTHUR L. L. (1904) Autoplastic sutures in hernia and other diastases. *JAMA* **43**, 1039–1048.

MCGAVIN L. (1909) The double-filigree operation for the radical cure of inguinal hernia. *Br. Med. J.* **2**, 347–363.

MAINGOT R. (1941) The floss silk lattice posterior repair operation for direct inguinal hernia. *Br. Med. J.* **1**, 777–778.

MAIR G. B. (1945) Preliminary report on the use of whole skin-grafts as a substitute for fascial sutures in the treatment of herniae. *Br. J. Surg.* **32**, 381–385.

MOLONEY G. E. (1948) Operations for hernia; technique of nylon darn. *Lancet* **2**, 45–48.

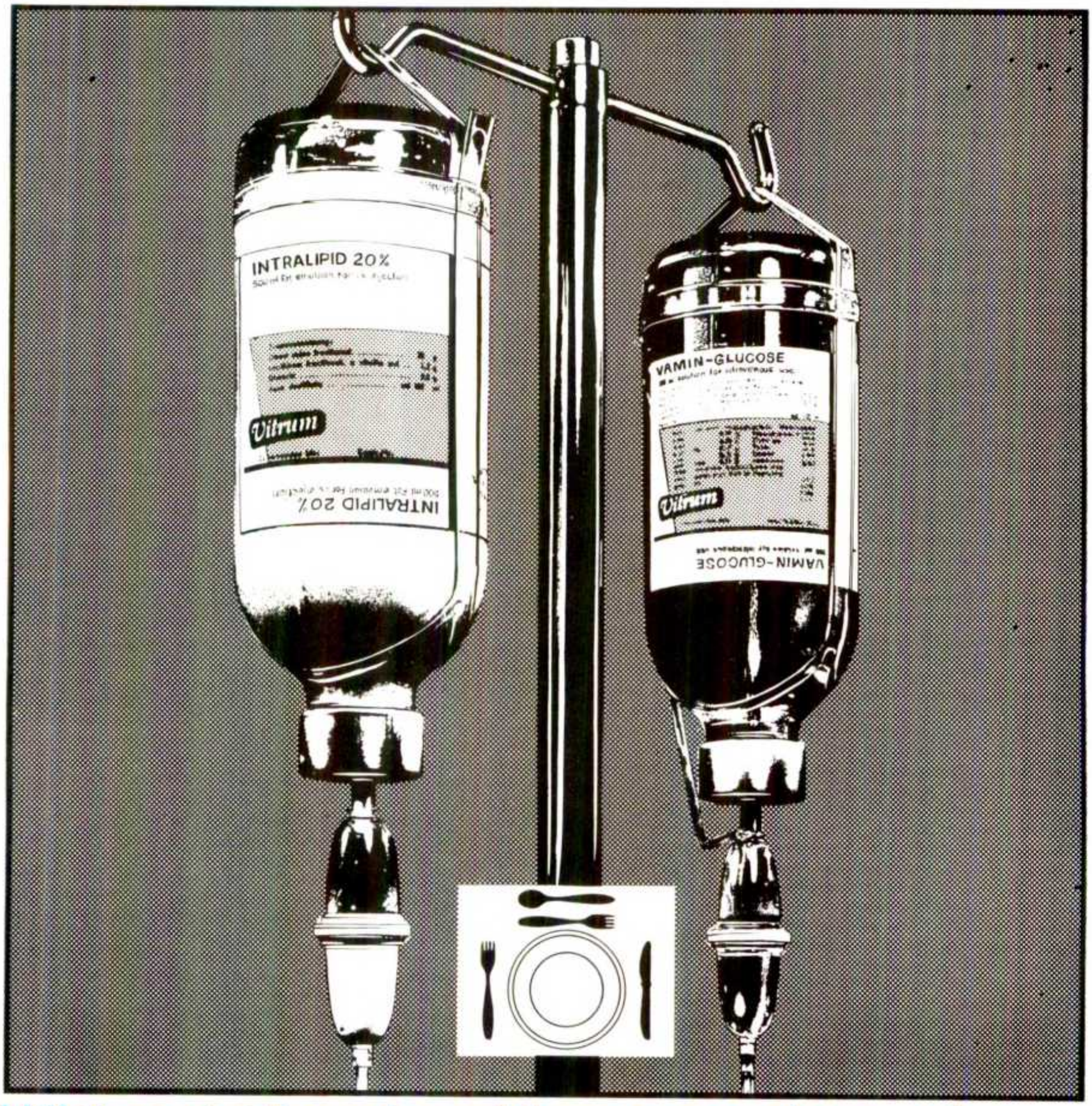
SAMES C. P. (1968) Vas deferens in hernioplasty. *Br. Med. J.* **3**, 744.

References
1. *Postgrad med J.* (1971) **47**. Supplement (September) 7.
2. *Brit med J.* (1972), **2**, 673.
3. *Clin Trials J.* (1972), **9**/**3**, 9.

SEPTRIN contains trimethoprim and sulphamethoxazole.
Full prescribing information is available on request.
Wellcome Medical Division.
The Wellcome Foundation Ltd.,
Berkhamsted, Herts.

When clinical examination reveals urinary infection in children, experience increasingly indicates the need for the prompt, vigorous action of SEPTRIN Paediatric Suspension.

Rated top oral treatment in a British survey of 23,491 urinary pathogen sensitivities,[1] SEPTRIN has been judged superior to ampicillin,[2,3] and is now well established as a first-line treatment for urinary infections.



With nutritional problems you always have solutions . . . *Vitrum* solutions

TOTAL PARENTERAL NUTRITION aids patient recovery. Improves wound healing. Increases resistance to infection. Fosters earlier discharge from hospital.

When the gastrointestinal route is inoperative nutrients must be supplied directly into the bloodstream. The total range of Vitrum solutions meets this requirement totally. Vitrum provides Total Parenteral Nutrition, in the forms and quantities naturally transferred to the bloodstream after digestion of normal food.

The body's requirement of aminoacids, the building stones of proteins, carbohydrates and electrolytes is provided by VAMIN and AMINOSOL solutions.

The requirement of energy, fat, essential fatty acids and phosphorus is provided by INTRALIPID.

VAMIN and AMINOSOL contain all the 18 aminoacids required for protein synthesis – essential, semi-essential and non-essential – in the physiological L-form.

✲Vamin/Glucose ✲Vamin-Fructose ✲Vamin "N"
✲Aminosol 10% ✲Aminosol/Glucose
✲Aminosol/Fructose-Ethanol
✲Intralipid 10% ✲Intralipid 20%

Vitrum = Nutritional Solutions

KabiVitrum

For full technical information write to the: Professional Services Division,
KabiVitrum Ltd., Bilton House, Uxbridge Road, Ealing, London W5 2TH
Telephone: 01-567 4717 or 01-579 1871

Br. J. Surg. Vol. 62 (1975) 497-500

Nitrogen mustard as adjunctive chemotherapy for breast carcinoma

JAMES R. HINES AND JOHN S. WILLIAMS

SUMMARY

A retrospective study is reported of 38 patients with breast carcinoma treated by radical mastectomy and a short course of nitrogen mustard. They were followed up for an average of 10 years. There were no serious untoward reactions to the drug. The 5- and 10-year corrected survival rates were 74 and 71 per cent respectively. There would appear to be a renewal of interest in adjuvant chemotherapy for patients with breast carcinoma.

POSTOPERATIVE adjunctive chemotherapy for patients with breast carcinoma is being reappraised. There have been at least 32 different studies using single drugs or combinations of drugs as adjuvant treatment in patients with 'surgically resectable' breast cancer and many new studies are in progress (Tormey and Geelhoed, 1975). Impetus for improved primary treatment of breast carcinoma comes from disappointment in the results of extended operations, pre- and postoperative irradiation, prophylactic oophorectomy and exogenous hormones. Immunotherapy has not yet had a significant impact as it is just beginning to be tried clinically.

While new trials using adjuvant chemotherapy are being started, there is a need to examine the results of earlier work in this area. This study reviews retrospectively the records of 38 patients who received a short course of nitrogen mustard as an adjuvant to radical mastectomy. These patients have been followed up for an average of 10 years. We can find only one other series in the English literature in which nitrogen mustard was used as the sole adjunctive chemotherapeutic agent in patients with breast carcinoma.

Patients and methods

The 38 female patients in this study had 'surgically curable' breast carcinoma as there were no cases with skin ulceration, chest wall fixation, fixed axillary nodes, distant metastases or inflammatory carcinoma. The ages of the patients ranged from 30 to 72 years, the average being 55 years. None of these patients had a serious associated medical illness. The size of the primary tumour ranged from 1 to 10 cm in greatest dimension, the average being 3 cm. All the tumours were adenocarcinoma of ductal origin. Thirteen of the 38 patients had one or more positive axillary lymph nodes.

All the patients were subjected to a standard Halsted radical mastectomy. The wounds were washed with a 50 per cent sodium hypochlorite (Dakin's) solution prior to skin closure in an effort to reduce local recurrence. Nitrogen mustard was given intravenously during the operation and on the first 2 postoperative days. The total dose was 0·4 mg/kg and each patient received an average of 7 mg a day for 3 days. Leucocyte and platelet counts were taken daily in 34 of the 38 patients. Patients with positive nodes received postoperative irradiation to the axillary, internal mammary and supraclavicular areas, the average total dose being about 7000 rad. Five patients, all premenopausal, were subjected to prophylactic oophorectomy shortly after mastectomy.

The postoperative follow-up was from 7 to 15 years, the average being 10 years. One patient was lost to follow-up after 50 months, but all of the others have been traced.

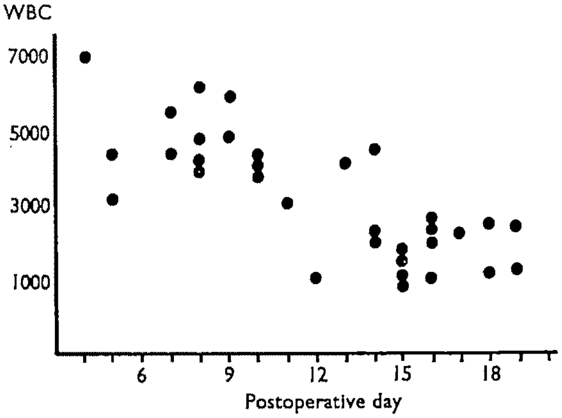


Fig. 1. Serial leucocyte counts in patients receiving NH$_2$ following mastectomy. Each dot represents the lowest count of a patient and the postoperative day that it was recorded.

Results

None of the patients in this series developed complications directly attributable to the chemotherapy. There were no deaths or serious postoperative morbidity. Wound problems occurred in 12 of the 38 patients (32 per cent). These were fluid collection in 6 patients, heavy crusting of the skin edges with slow healing in 3 patients, necrosis of skin requiring grafting in 2 patients and scar formation requiring plastic correction in 1 patient. These complications are similar in type and degree to those found in most series of patients with radical mastectomy with chemotherapy (Cohn et al., 1968). No significant depression of platelet counts was noted. Leucocyte depression was common, the lowest count being 900/ml. The lowest white blood cell counts were from the twelfth to the

---

* Department of Surgery, Northwestern University Medical School, Chicago, Illinois.

Table I: HISTOLOGY OF THE TUMOURS

Tumour type	No. of patients	No. died
Poorly differentiated scirrhous carcinoma	16	4
Poorly differentiated adenocarcinoma	5	3
Well-differentiated scirrhous carcinoma	4	0
Well-differentiated adenocarcinoma	3	1
Poorly differentiated mucinous carcinoma	2	0
Well-differentiated medullary carcinoma	2	0
Well-differentiated mucinous carcinoma	1	1
Well-differentiated intraductal carcinoma	1	0
Undifferentiated carcinoma	1	1

Table II: NODAL STATUS OF THE PATIENTS

No. of positive nodes	No. of patients	No. died	% survived
0	24	3	87·5
1–3	2	1	50
4 or more	9	6	32

eighteenth day and the average count on the fifteenth postoperative day was 2030/ml (*Fig.* 1). After this time a gradual rise toward normal was seen and the counts had returned to normal by the thirtieth day. Reverse isolation was used when the white cell count went below 2000/ml.

One patient was lost to follow-up at 50 months. At that time she was clinically free of her tumour. Two patients died of unrelated diseases, one at 34 months and one at 50 months; both patients were clinically free of breast carcinoma at the time of their death. Thus, 35 patients were available for long term follow-up. Two patients developed carcinoma in the opposite breast, one at 6 years and one at 7 years. Both are still alive 5 and 7 years later, following a second mastectomy. Local skin recurrences were detected in 2 patients, one at 1 year and one at 4 years. The first patient is still alive 7 years later, but the second died of disseminated disease. Two patients developed isolated bone lesions presumed to be metastases, one in a pelvic bone 4 years after mastectomy and one in a rib 4 years after mastectomy. Both were treated by irradiation and are alive 6 and 7 years later respectively. Four of the 5 patients subjected to prophylactic or adjunctive oophorectomy are alive and well. Two of these patients had the isolated bone lesions.

Ten of the 35 patients followed up died of breast carcinoma. The other 25 patients (71 per cent) are alive and clinically free of breast cancer at this time. Of the deaths, 9 patients died within 5 years and one died 10 years following mastectomy. The average time from mastectomy to death was 42 months. The patients with the more undifferentiated tumours had a somewhat lower rate of survival (*Table I*). The patients with positive lymph nodes had a markedly reduced survival rate (*Table II*).

The crude 5-year survival rate was 68 per cent and the adjusted 5-year survival rate was 74 per cent. The crude 10-year survival rate was 65 per cent and the adjusted 10-year survival rate was 71 per cent.

Discussion

The principle of adjuvant chemotherapy is based on two experimental observations. In animals, cure of implanted carcinoma has been achieved following subtotal tumour resection and simultaneous administration of chemotherapeutic agents. In addition, chemotherapeutic agents were effective in preventing the 'take' of injected tumour cells (Cruz et al., 1956; McDonald et al., 1956, 1957). Circulating tumour cells have been demonstrated in the bloodstream of patients with various forms of malignancy. The number of these tumour cells increases during periods of surgical manipulation (Roberts et al., 1961; Evans and Scott, 1969). The objective of adjuvant chemotherapy is both the prevention of implantation of circulating tumour cells and the possible eradication of early metastases.

During the mid-1950s many investigators began clinical trials of adjuvant chemotherapy in the surgical treatment for breast carcinoma (Shimkin and Moore, 1958; Holland, 1961; Roberts et al., 1961; Noer, 1963; Fisher et al., 1968; Donegan, 1970; Mrazek and McDonald, 1970; Nissen-Meyer, 1970; Finney, 1971; Fisher, 1971; Nissen-Meyer et al., 1971; Donegan, 1974). Results varied from markedly optimistic, especially during the early phases of the studies (Mrazek and McDonald, 1970), to those showing decreased survival and increased recurrence compared with control groups (Finney, 1971). In most of the studies single agent, short-term, postmastectomy chemotherapy did little to alter the long-term survival in breast carcinoma. The major investigation, undertaken by the National Institutes of Health National Surgical Adjuvant Breast Project (NSABP) involving 23 separate institutions over a 10-year period, was reported by Fisher et al. in 1968. A total of 1341 patients in the project received thiotepa, 5-fluorouracil or a placebo. They found that a 3-day course of postoperative thiotepa to be of benefit only to premenopausal women with four or more histologically positive axillary lymph nodes. The 5-year survival rate in this group was 58 per cent, and was 25 per cent in the controls. They also found that thiotepa seemed to have the same inhibitory effect on local recurrence that is seen with postoperative radiotherapy.

Tormey and Geelhoed (1975) quoted a Russian study reporting a lowered recurrence rate following 2 weeks of postoperative thiotepa. They also reported that a German study using oral cyclophosphamide for 2 months effectively reduced recurrence, and a study from a Scandinavian group using cyclophosphamide also gave good early results. Mrazek and McDonald (1970) gave nitrogen mustard at the time of operation and every 3 months for several courses of treatment. They found a reduced recurrence rate, especially in premenopausal patients with negative axillary nodes. This is the only study we have found in which nitrogen mustard was used as the sole adjuvant drug in the primary treatment of breast carcinoma.

The long term use of adjuvant chemotherapy with thiotepa has been reported by Long et al. (1969) and Donegan (1970, 1974). They gave weekly injections and have reported a trend towards improved survival in patients with negative axillary nodes. The NSABP is organizing a trial of long term chemotherapy with phenylalanine nitrogen mustard as an adjuvant to radical mastectomy in patients with four or more positive axillary nodes (Fisher, 1972).

Combination chemotherapy has had encouraging results in patients with metastatic breast carcinoma (Carter, 1972). Protocols for adjuvant chemotherapy with a combination of drugs are being developed by several groups including the Eastern Oncology Group, Acute Leukemia Group B, the Mayo Clinic and Berto Verici in Milan. Another intriguing possibility that has been suggested is the combination of chemotherapy and immunotherapy. Chemotherapy would serve to decrease the number of tumour cells prior to the initiation of immunotherapy (Fisher, 1972).

The current study of 38 patients is too small to provide evidence for or against adjuvant chemotherapy in breast carcinoma. The 71 per cent survival rate with an average follow-up of 10 years is above the average 5- or 10-year survival rates (Butcher, 1961; Goldenberg et al., 1961). This survival rate may have been favourably influenced by aggressive postoperative follow-up care. The incidence of complications in this series was no greater than that seen in patients having radical mastectomy without chemotherapy, and there was no significant patient discomfort or increased hospital stay associated with the treatment. While the use of nitrogen mustard did not prevent the use of other forms of adjuvant therapy—irradiation and oophorectomy—it has the potential for causing serious untoward effects.

Nitrogen mustard (mustargen hydrochloride, NH$_2$) is the parent compound of all the alkylating agents and one of the first chemotherapeutic agents found to be effective against tumour cells. Alkylating agents affect tumour cells (and to a lesser extent normal cells) by disturbing DNA synthesis during cell division through a process of misreplication of the DNA chains (Finney, 1971). HN$_2$ has the disadvantage of requiring intravenous administration because of its vesicant properties, but this caused no problem in the present series as all the patients were hospitalized and were given a short course of treatment. NH$_2$ has been shown to be effective in the treatment of metastatic breast carcinoma (Holland, 1961; Carter, 1972). Immediate undesirable reactions of NH$_2$ include anorexia, nausea and vomiting. Long term untoward effects include leucopenia, thrombocytopenia, allergic rash, infection with herpes zoster and menstrual irregularities. Phlebitis, skin slough and severe brawny induration have been seen following local infiltration of the drug. Nitrogen mustard can cause serious problems. A patient in our institution died of leucopenia and thrombocytopenia following its administration as adjuvant chemotherapy. In a nearby hospital a subcutaneous extravasation of NH$_2$ caused a skin slough that required extensive skin grafting. While the untoward effects of nitrogen mustard have limited its use as an adjuvant agent, the studies using this drug are so few that we feel even this small series should be reported.

The value of adjuvant chemotherapy in breast carcinoma is not known. Bernard Fisher, one of the principal investigators in the NSABP study, feels that the trials to date do not repudiate the value of adjuvant chemotherapy, but simply provide 'no test' (Fisher, 1972). Because of increased understanding of tumour pathology, tumour–host relationships, the mechanism of chemotherapeutic agents and the development of new drugs, new trials should be undertaken. While renewed interest appears warranted, it is still an experimental procedure. Only by well-planned, cooperative, prospective clinical trials can the value of this treatment be obtained in a reasonable period of time. Surgeons should join these trials if there is a possibility of long term benefit to the patients and the treatment has a low incidence of toxicity. Dr Douglas C. Tormey, Chief of the National Cancer Institute's Medical Breast Cancer Service, said in March 1974: 'Current estimates suggest that micrometastases are present with a breast mass' and that animal studies strongly suggest 'it is much easier to eradicate early micrometastases than it is for them to become clinically manifest'.

References

BUTCHER H. R. jun. (1961) Effectiveness of radical mastectomy for mammary cancer: an analysis of mortality by the method of probits. *Ann. Surg.* **154**, 383–396.

CARTER S. jun. (1972) Single and combined non-hormonal chemotherapy in breast cancer. *Cancer* **30**, 1543–1555.

COHN I., SLACK N. and FISHER B. (1968) Complications and toxic manifestations of surgical adjuvant chemotherapy for breast cancer. *Surg. Gynecol. Obstet.* **127**, 1201–1209.

CRUZ E, MCDONALD A. and COLE W. (1956) Prophylactic treatment of cancer, the use of chemotherapeutic agents to prevent tumor metastases. *Surgery* **40**, 291–296.

DONEGAN W. L. (1970) Prolonged surgical adjuvant chemotherapy with Thio-TEPA for mammary carcinoma. *Tenth Int. Cancer Congr.* (Abstr.), p. 500.

DONEGAN W. L. (1974) Extended adjuvant chemotherapy for mammary carcinoma. *Central Surgical Assoc., 21st Annual Meeting, Cincinnati, Ohio, March 1974.*

EVANS H. J. and SCOTT D. (1969) The induction of chromosome aberrations by nitrogen mustard and its dependence on DNA synthesis. *Proc. R. Soc. Lond.* (*Biol.*) **173**, 491–512.

FINNEY R. (1971) Adjuvant chemotherapy in the radical treatment of carcinoma of the breast—a clinical trial. *Am. J. Roentgenol.* **111**, 137–141.

FISHER B. (1971) Status of adjuvant therapy: results of the national surgical adjuvant breast project studies on oophorectomy, post-operative radiation therapy and chemotherapy. *Cancer*, **28** 1654–1658.

FISHER B. (1972) Surgical adjuvant therapy for breast cancer. *Cancer* **30**, 1556–1564.

FISHER B., RAVDIN R. G., AUSMAN R. K., SLACK M. H., MORE G. E. and NOHR R. J. (1968) Surgical adjuvant chemotherapy in cancer of the breast. *Ann. Surg.* **168**, 337–356.

GOLDENBERG I. S., BAILAR J. C., HAYES M. A. and LOWERY R. (1961) Female breast cancer: a re-evaluation. *Ann. Surg.* **154**, 397–407.

HOLLAND J. F. (1961) Chemotherapy and chemopraxis of cancer, 1961. *Cancer Res.* **21**, 1086–1099.

LONG R. T., DONEGAN W. L. and EVANS A. M. (1969) Extended surgical chemotherapy for breast carcinoma. *Am. J. Surg.* **117**, 701–704.

MCDONALD G. O., CRUZ E. P. and COLE W. H. (1956) The effect of cancer inhibitor drugs on the "take" of Walker carcinosarcoma 256 in rats. *Surg. Forum* **7**, 486–489.

MCDONALD G. O., LIVINSTON C., BOYLE C. R. and COLE W. H. (1957) The prophylactic treatment of malignant disease with nitrogen mustard and triethylenethiophosphromide (Thio-TEPA). *Ann. Surg.* **145**, 624–629.

MRAZEK R. G. and MCDONALD G. O. (1970) Surgery and adjuvant chemotherapy in treatment of Breast carcinoma. *Tenth Int. Cancer Congr.* (Abstr.), p. 501.

NISSEN-MEYER R. (1970) Preliminary report from the Scandinavian adjuvant study group. *Tenth Int. Cancer Congr.* (Abstr.), p. 499.

NISSEN-MEYER R., KJELLGREN K., and MANSSON B. (1971) Preliminary report from the Scandinavian adjuvant chemotherapy study group. *Cancer Chemother. Rep.* **55**, 561–566.

NOER R. J. (1963) Adjuvant chemotherapy. Thio-TEPA with radical mastectomy in the treatment of breast Cancer. *Am. J. Surg.* **106**, 405–412.

ROBERTS S., JONASSON O., LONG L., MCGRATH R., MCCREW E. and COLE W. (1961) Clinical significance of cancer cells in the circulating blood. *Ann. Surg.* **154**, 362–371.

SHIMKIN M. B. and MOORE C. E. (1958) Adjuvant use of chemotherapy in the surgical treatment of cancer: plan of cooperative study. *JAMA* **167**, 1710–1714.

TORMEY D. C. (1974) Cancer therapy: how you can gauge adequacy of treatment. *Med. Wld News*, 17 May, pp. 38–44.

TORMEY D. C. and GEELHOED G. W. (1975) Current concepts in the management of breast carcinoma. *Contemporary Surg.* **5**, 9.

Br. J. Surg. Vol. 62 (1975) 501–504

Reviews and notices of books

Functional Anatomy of the Digestive System
R. M. H. McMinn, London, and M. H. Hobdell, London. 240×185 mm. Pp. 239+xi. Illustrated. 1974. Tunbridge Wells: Pitman Medical. £2·90.

MODERN preclinical education has two important features. First, it tries to break down the rigid barriers between the various disciplines which make up the student's curriculum; this simplifies and rationalizes the enormous amount of material he must ingest during his undergraduate career. Secondly, it attempts to select and emphasize the topics which the student is going to need in the clinical part of his course and in his subsequent career. This volume achieves both these commendable targets. It considers the digestive tube and its adnexa from anatomical, histological, developmental and physiological aspects, emphasizing wherever possible the practical applications of basic sciences. In the section on the mouth, the teeth have been considered in some detail for the benefit of dental students, Dr Hobdell being an experienced teacher of dental anatomy. The text includes descriptions of surface markings, normal radiography and the techniques of investigating the various components of the alimentary tract. The book is clearly written and produced, and is copiously illustrated by line diagrams, together with histological and electron-microscopic photographs.

This is a book which can be recommended without hesitation to medical and dental students. The reviewer's only regret is that it was not available to him 31 years ago. HAROLD ELLIS

Atlas of Human Anatomy. Volumes 1, 2 and 3
Edited F. H. T. Figge and W. J. Hild. Ninth English edition. Based on the seventeenth German edition edited by H. Ferner and J. Staubesand. 250×200 mm. Pp. 275+xvi, 245+xvi and 357+xx, with 365, 315 and 443 illustrations respectively. 1974. München: Urban & Schwarzenberg. DM 75, 75 and 85.

THIS is the ninth edition in English of the *Atlas of Human Anatomy*, largely supervised by Professor F. H. T. Figge of Baltimore before he died and completed in the emergency by Professor W. J. Hild of Galveston. There is a companion seventeenth edition in German.

The continued popularity of this book speaks for itself. The English edition is obviously more used in America than in the United Kingdom and this is a measure of the curtailment of work in American dissecting rooms and an indication of how most anatomical museums have been transformed into laboratories devoted to ultrastructure and not to gross structure. There are sufficient plates of different levels of exposure in most regions to make the surgeon familiar with what to expect as the way opens up before his scalpel.

Without doubt the price will deter most British undergraduate students, but the book's continued presence in college libraries and postgraduate centres will ensure its justified popularity.

Volume 1 is concerned with the locomotor system in general. There could probably have been more X-rays of bones and joints and ossification is rarely mentioned. The diagram of the muscle attachments in the hand (*Fig.* 326) is difficult to follow, but that of the foot (*Fig.* 354)—well, words fail.

Volume 2 is concerned with visceral anatomy. Variations in shape and position are illustrated with X-rays, and the surgeon will find the illustrations of the commoner arrangements of the extrahepatic biliary system useful. The X-rays are of a very good standard and are well reproduced. Some are unusual, as of the seminal vesicles and the ducti deferentia viewed against an air-filled urinary bladder! The three-dimensional low power histological photomicrographs of the wall of the different regions of the alimentary tract are very helpful.

Volume 3 is concerned with the nervous system, skin, etc. This volume contains an Errata insert—mostly of names which had not been changed from the Latin or the German into English. Brain plates are very standard. The diagrams of cortical localization by Brodmann and by Foerster have been retained and there are summaries of the main afferent and efferent pathways. The section on the autonomic nervous system is short and not very helpful. There is a jungle of sympathetic fibres. The cranial parasympathetic ganglia are shown along with the peripheral nerves. The pelvic parasympathetic nerves could not be found anywhere.

J. T. AITKEN

Endoscopy of the Small Intestine with Retrograde Pancreatocholangiography
Edited L. Demling and M. Classen, Erlangen. 230×155 mm. Pp. 143+xi, with 114 illustrations. 1974. Stuttgart: Georg Thieme Verlag. DM.38.

THE ideas formulated at the International Workshop on Enteroscopy in July 1972 at Erlangen are recorded in this book in abridged form.

The first part of the book deals with the duodenum and papilla of Vater. This opens with a helpful paper on the diagnosis of duodenal ulcer with various fibrescopes and goes on to discuss questions in non-ulcer duodenopathy ('duodenitis'). Some more unusual subjects are then discussed, such as islands of gastric mucosa in the duodenum and malignant tumours of the upper small intestine.

The second part of the book is concerned with the pancreas, with the technical problems of retrograde pancreatography and the difficulty in diagnosing tumours and chronic pancreatitis. There are useful papers on evaluation of angiography and pancreatography in radiological diagnosis of pancreatic diseases, and an interesting article on duodenoscopic collection of intraductal pure pancreatic juice and its application to cytodiagnosis. There is also a paper on the hazards of endoscopic retrograde cholangiopancreatography. The brief paper on endoscopy in the diagnosis of obstructive jaundice is particularly useful. Inspection of the small bowel from above and below is adequately dealt with.

Progress of endoscopy in the past 10 years has been truly remarkable and this book represents a useful summary of the present position. IAN MCCOLL

Abdominal Echography. Ultrasound in the Diagnosis of Abdominal Conditions
E. Barnett and P. Morley, Glasgow. 216×140 mm. Pp. 138+x. Illustrated. 1974. London: The Butterworth Group. £4·50.

THIS little paperback book encompasses the immense experience of the authors in the art of sonar techniques. The illustrations almost exceed the text in quantity and are masterpieces of clarity. The techniques of obtaining ultrasonograms and the basis for interpreting them are made clear in a way which leaves the reader with no lingering doubts. The diagnostic uses available to the gynaecologist, obstetrician, internist, general surgeon and urologist are all concisely covered. Every new subject produces its own terminology and a useful glossary is provided to help and instruct the beginner.

Now that higher qualifications in diagnostic radiology demand knowledge of sonar methods, aspirants would be well advised to take the opportunity of assimilating the knowledge here presented in such palatable form. Considering the very large number of illustrations the price of this book must be regarded as reasonable. IAN DONALD

General Ophthalmology

Daniel Vaughan, San Francisco, and Taylor Asbury, Cincinnati. Seventh edition. 260 × 180 mm. Pp. 334. Illustrated. 1974. Los Altos, California: Lange Medical Publications. $9.50.

THE seventh edition of this interesting book is of value to medical students in that a wide range of ocular disorders is described, albeit in most instances briefly. This brevity of description detracts from the quality of the book as it must leave too many questions unanswered, even for medical students. For consultant and trainee ophthalmologists the book is not of academic interest. The illustrations, all in black and white, are excellent and numerous and give the reader a clear view of the disorder. There are abundant line drawings which are utilized to augment the text and they are particularly welcome in the anatomical introduction to chapters. In the appendices, of which there are three, the second contains good descriptions of common ophthalmic drugs which the student will find helpful, while the tables should also aid memorization of their contents. It is perhaps a pity that a longer description of the Goldmann perimeter and the interpretation of its fields are not included. The reasonably up-to-date text is clearly printed in double columns on good quality paper.

I. M. DUGUID

Safe Central Venous Nutrition. Guidelines for Prevention and Management of Complications

Mohamad H. Parsa, José M. Ferrer and David V. Habif, New York. 230 × 150 mm. Pp. 266+xi, with 131 illustrations. 1974. Springfield, Ill.: Charles C. Thomas. No price given.

THIS book describes the experience of the authors of intravenous feeding at the Harlem Hospital during a period of 4 years. A central venous catheter was inserted 3059 times in more than 2000 patients of whom 400 were fed in this way with solutions of amino-acids or a protein hydrolysate and dextrose solution; fat was not used because it was not available in the United States at the time. They describe their techniques for the insertion of catheters into various veins and the treatment of the complications that they caused. There are a number of diagrams and photographs of the methods of inserting a cannula into the subclavian and other veins, but it is a pity that the operator only wears gloves and does not emphasize the strict aseptic precautions which seem desirable if infection is to be reliably prevented. The complications are listed; they occurred at a rate of 3·53 per cent per catheter, and of the 41 due to infection, septicaemia occurred in 36. Of the 118 references, 85 per cent were published in North America. There is no discussion at all of the use of fat emulsions and this serious omission greatly reduces the value of this book to those who work in countries where commercial fat emulsions are available. Moreover, the practice of transferring solutions from one bottle to another and of adding vitamins and electrolytes which is illustrated as well as described is contrary to the Federal Drugs Administration's hallowed and good principle of 'sterile in the final container'. There is useful information in this book but it is otherwise of limited value to the British reader.

A. W. WILKINSON

Chirurgie der Gegenwart

Edited R. Zenher, München, F. Deucher, Aarau, and W. Schink, Köln. 260 × 180 mm. Vol. 1, pp. 11, 22. Vol. 3, pp. 64, 34, 37. Vol. 4, pp. 46, 46. Illustrated. 1974. München: Urban & Schwarzenberg. No price given.

FURTHER chapters of this multivolume loose-leaf surgical text have now appeared. Carstensen has written about acid base balance and Bregulla and Ober have contributed a most useful chapter about the relationship between general surgical conditions and pregnancy. Accidents, appendicitis, hernias and other problems associated with pregnancy are discussed and treatment is evaluated.

In the orthopaedic volume Weber discusses the treatment of trauma to the ankle and the proximal part of the foot. Wstrow considers injuries to the nose and frontobasal fractures and the latter chapter has an up-to-date list of references.

Volume 3 dealing with thoracic surgery has also appeared and the first chapters include diagnostic measures, the surgery of the mediastinum and benign tumours of the lungs. All the chapters are exceedingly well illustrated and Professor Zenker and his colleagues should be congratulated on the speed with which the chapters of this mammoth work are appearing. The final assessment must await the completion of these seven volumes.

H. B. ECKSTEIN

Corticosteroid and ACTH Treatment. Principles and Problems

A. B. Myles, Surrey, and J. R. Daly, London. 226 × 115 mm. Pp. 216+viii. 1974. London: Edward Arnold. £4·75.

THIS is a well-written and readable book that in only 200 pages gives sufficient information about the chemistry, physiology and pharmacology of corticosteroids and corticotrophin to enable doctors to treat their patients with awareness of the problems involved in their use.

Various minor disagreements with the text could be mentioned, e.g. is the zonation of the human adrenal cortex really as clearcut as is suggested (p. 20)? Labelled cortisol should not be given by mouth for measurement of secretion rate (p. 31). Tetracosactrin tests should be performed at 8–10 a.m., when plasma cortisol is high (p. 40). More serious objection could be made to the use of dextrose–saline solutions in the treatment of adrenal insufficiency. These patients are depleted of extracellular fluid and have difficulty in excreting water. They must therefore be given 0·9 per cent sodium chloride solution and may require large volumes, e.g. 10 litres, to restore their volume depletion. The addition of deoxycorticosterone does not really help in these circumstances; recovery is quicker if more frequent (i.e. 4-hourly) intravenous injections of hydrocortisone sodium succinate are given.

In the section on treatment the authors correctly stress the efficiency of glucocorticoids in the early stages of rheumatoid arthritis and the danger of its use in the later stages where the physician may find himself trapped into giving larger and larger doses to relieve pain, with the eventual development of serious complications. In these circumstances other forms of treatment should be sought, although these also have their risks. Little exception can be taken to their suggestions for the management of patients with various diseases in which caution is shown in their advice as to dosage and awareness as to the effects of prolonged overdosage.

Overall, a volume giving adequate background to the use of these valuable but dangerous forms of therapy in an informed manner—as such, it should find a place on every doctor's desk.

E. J. ROSS

Modern Trends in Paediatrics—4

Edited John Apley, Bristol. 220 × 150 mm. Pp. 376+x. Illustrated. 1974. London: The Butterworth Group. £7·50.

THERE is a good deal in this book of value as well as of interest to any surgeon who has to deal with children. There are chapters on food and the fetus, growth of the fetus and the effects of drugs in fetal life and infancy, indicating how interest is steadily shifting to earlier stages of human development. The rapidly expanding field of antenatal diagnosis is also discussed and the present scope and future possibilities are assessed. There are other provocative and stimulating chapters on the treatment of acute lymphoblastic leukaemia, cystic fibrosis, the assessment of renal function, endocrinology, immunobiology and the emotional aspects of injury in children. Although it is becoming less common, hypertrophic pyloric stenosis remains an important problem for the surgeon and there is a good review of recent work, but the aetiology is still wrapped in mystery and confusion. There is also a discussion of learning, teaching and training in paediatrics and an excellent final chapter on ethical problems which should be read by everyone who has to treat children. This is a well-produced and easily read book and the editor is to be congratulated on the palatable and interesting mixture that he has achieved.

A. W. WILKINSON

Diseases of the Ear

Stuart R. Mawson, London. Third edition. 225×150 mm. Pp. 584+vii, with 286 illustrations. 1974. London: Edward Arnold. £18·50.

In this country all otologists are practising otorhinolaryngologists, although gradually there has been a tendency for a few particularly talented individuals to concentrate almost exclusively on this single facet of an increasingly expansive speciality. The author, as a member of this select fraternity, is therefore uniquely placed to write what has now become a standard textbook on the ear. The two previous editions were excellent and this, the third, is superb! It is obvious that the 7 years which have elapsed between editions has been spent by Mawson in an intensive reappraisal of his text together with a searching analysis of the new published material. These years have seen a dramatic change of emphasis in otology. The idol of technical expertise has been partially replaced by an awareness of the need for greater scientific understanding of the ear as a functioning unit. Unfortunately, owing to lack of financial support and interest, little of this work has emanated from this country. However, everything of practical importance is included in the third edition, making it not only ideal for the examination candidate but essential for all thoughtful otologists. The book remains compact both in page size and bulk—evidence of vigorous pruning and an understanding publisher. Since the text is all-embracing with nothing of importance left out, there is little purpose in reproducing a list of contents. The number of informative yet simple tables has been greatly increased and once again this is witness to the fact that the author is an experienced practical otologist with more than a passing interest in teaching. The section on operative surgery, which cannot offer adequate instruction to those who are really in need, may inadvertently make an intricate procedure appear deceptively simple!

The line drawings, as in previous editions, are the work of yet another otologist, and contribute more than is usual to the text. Even the clinical photographs, unfortunately in black and white, suffer less than is expected by the necessity for a drastic reduction in size for publication. There is little to criticize and much to admire. Whatever the price this book is worth the money, for, if nothing else, it indicates that with the right person, subject and publishers this country can still produce an outstanding medical book.

D. F. N. HARRISON

Surgical Treatment of Head and Neck Tumours

Edited Jorge Fairbanks Barbosa, São Paulo, Brazil. 280×215 mm. Pp. 311+xiii. Illustrated. 1974. New York: Grune & Stratton. £16.

This book is written by the senior staff of the head and neck service of the cancer centre of São Paulo, Brazil. The editor is a major contributor. One chapter on cancer of the middle ear is contributed by Professor Conley of New York, who also wrote the Foreword.

The contents constitute a testament of the current practice of the authors in the cancer centre in which they work. The work is not an attempt at an encyclopaedic statement of all surgical techniques available to the surgeon engaged in this field. The possible disadvantages of omission which this format entails are more than compensated by the authenticity of the writing by all the contributors. It is at once apparent to the reader that he is being given information clearly and in detail about methods in day-to-day use to meet varying clinical situations and which have been found to work. No omnipotence is claimed or implied, which is refreshing; one feels that one can disagree about detail here and there without offending.

The subject is very fully covered and the translation has been so well made that the spontaneity of the text has not been lost. The book is profusely illustrated with drawings of masterly clarity which greatly enhance its value to students of all levels of experience. The basic principles of radical excision and of reconstruction to meet functional and aesthetic requirements are repeatedly stated, together with sound common sense of the many needs, other than surgical, of patients so severely afflicted. Human understanding and surgical expertise are well blended.

The editor, in his preface, states that the naming of techniques after individual surgeons has been deliberately avoided for fear that an injustice might be done, but many names are mentioned in the text and it is a serious omission that no references are given at the end of any chapter. The index could also be enlarged for ease of reference by the reader, or more detail could be given beneath the chapter headings in the list of contents. The book is well produced, and it is a pity that an error in the binding of the reviewer's copy resulted in omission of half the index. It is possible that a list of references at the end of the book was also omitted by this error.

DAVID MATTHEWS

Current Pediatric Diagnosis and Treatment

Henry Kempe, Henry K. Silver, Donough O'Brien and associate authors. Third edition. 260×185 mm. Pp. 1020. Illustrated. 1974. Los Altos, California: Lange Medical Publications. $12.

This is the third edition of a well-known textbook. It aims to deal with principles of diagnosis and treatment in a way which will satisfy the requirements of the medical student and the paediatrician in the early stages of his training. It also tries to detail clinical methods and procedures in an implied attempt to be encyclopaedic. This is possibly the reason why, in spite of the immense amount of information which this book provides, one is left with rather a breathless feeling, but this may be unfair and unduly critical. It must be said that at a price of $12 a thousand pages seems good value, and the 51 authors cover a vast number of subjects. The opening chapters on history and physical examination are more a comprehensive catalogue than a discussion of how to go about obtaining a history and examining a baby, and perhaps this is right and a modern way to do it, but a bit more of fatherly advice might serve the student better.

A surgeon might be forgiven for feeling disappointed at the short shift given to both osteomyelitis and pyelonephritis in the newly born and even more so at the repetition of the advice to instil opaque medium into the upper pouch of the oesophagus to make the diagnosis of oesophageal atresia. In later sections the various causes of neonatal intestinal obstruction are described, but more cross references would be helpful, especially with the chapter on the neonate. Meconium plug obstruction is much more likely to be cleared by a Gastrografin than a barium enema. There are some diagrams and many tables some of which are very useful but more illustrations would be of value.

A. W. WILKINSON

Tumors of the Esophagus and Stomach

S-Chun Ming, Pennsylvania. 260×203 mm. Pp. 279. Illustrated. 1973. Washington: Armed Forces Institute of Pathology. No price given.

This book is a section of the *Atlas of Tumor Pathology* under the general editorship of Harlan I. Firminger and assisted by a very distinguished editorial advisory committee.

Every conceivable tumour of the oesophagus and stomach is described in great detail and the text is profusely illustrated; a number of the illustrations are in colour. For purposes of reference this book is invaluable and every care has been taken to give a proper sense of proportion to the rare conditions which are included. Perusal of the book, however, shows that this is much more than a book of reference. For example, the section on epidemiology and geographic incidence of cancer of the oesophagus gives a short but well-balanced account of the current views held on this aspect of the disease. Similarly, the controversial opinions regarding the relationship between chronic gastric ulcer and gastric carcinoma are summed up in a masterly way. The account of the conditions associated with cancer of the oesophagus is short but clear.

The contemporary bibliography is excellent but the interest of the reader could have been increased by the inclusion of the accounts of some of the earlier writers. This book should be read by all surgeons with a serious interest in tumours of the oesophagus and stomach and the author is to be congratulated on having made a major contribution to the subject.

R. H. FRANKLIN

Book notices

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and those having the greatest interest to our readers.]

International Awards for Biomedical Research and Research Training, National Institutes of Health, Fiscal Year 1973
Prepared by Internation Cooperation and Geographic Studies Branch, Fogarty International Center. 204 × 268 mm. Pp. 87+vi. 1974. Maryland: US Department of Health, Education and Welfare. No price given.

Cerebral Vascular Disease
Edited J. S. Meyer, H. Lechner, M. Reivich and O. Eichhorn. 230 × 155 mm. Pp. 280+xvi, with 108 illustrations. 1974. Stuttgart: Georg Thieme Verlag. DM.42.

Face au cancer du sein. Actualités, 1973
Jacques Reynier et al. 210 × 270 mm. Pp. 132, with 141 illustrations. 1974. Paris: L'Expansion Scientifique Française. 83F.

Les Entretiens de Bichat 1974
Edited P. L. Chigot, A. Bellin and D. J. Duché. 224 × 174 mm. Pp. 495. 1974. Paris: L'Expansion Scientifique Française. 14.60F.

The Knee Joint. Recent Advances in Basic Research and Clinical Aspects
Edited by O. S. Ingwersen, Eindhoven, B. Van Linge, Rotterdam, Th. J. G. Van Rens, Nijmegen, G. E. Rosingh, Haarlem, B. E. E. M. J. Veraart, Arnhem, and D. Le Vay, Withyham, Sussex. 240 × 165 mm. Pp. 329+ix. Illustrated. 1974. Amsterdam: Excerpta Medica North-Holland. $30.80.

Rekonstruktive chirurgie der Arterien
Jorg Vollmar, Ulm. 260 × 175 mm. Pp. 451+xvi, with 353 illustrations. 1974. Stuttgart: Georg Thieme Verlag. DM.184.

Les Fractures du Cotyle
Robert Judet and Emile LeTournel, Paris. 250 × 190 mm. Pp. 336, with 235 illustrations. 1974. Paris: Masson et Cie. 280F.

Les Complications Digestives du Stress
A. Sibilly, Strasbourg, and Ph. Boutelier, Paris. 240 × 160 mm. Pp. 158. Illustrated. 1974. Paris: Masson et Cie. 50F.

Embolies Pulmonaires
P. Marion, Lyon, and J. P. Binet, Paris. 240 × 160 mm. Pp. 160. Illustrated. 1974. Paris: Masson et Cie. 50F.

Poly (ADP-Ribose). An International Symposium
Edited Maureen Harris. 230 × 145 mm. Pp. 337+x. Illustrated. 1974. Maryland: US Department of Health, Education and Welfare. $5·65.

Techniques Chirurgicales du Pied
B. Regnauld. 250 × 170 mm. Pp. 185+xi, with 238 illustrations. 1974. Paris: Masson et Cie. 192 F.

Technik der Harnstein-analyse
H. J. Schneider, Jena. 270 × 185 mm. Pp. 166, with 112 illustrations. 1974. Leipzig: Veb Georg Thieme. M.84.

Volume 15 Urologie
R. Couvelaire and J. Cuckier, Paris. 250 × 185 mm. Pp. 848, with 993 illustrations. 1974. Paris: Masson et Cie. 335F.

Nouveau Traité de Technique Chirurgicale
Volume 6. Membres et Ceintures, Généralités Membres Supérieurs
R. Merle d'Aubigne and F. Mazas, Paris. 250 × 185 mm. Pp. 752, with 623 illustrations. 340F.

Obstetrics Illustrated
M. M. Garrey, A. D. T. Govan, C. Hodge and R. Callander, Glasgow. Second edition. 245 × 190 mm. Pp. 538. Illustrated. 1974. Edinburgh: Churchill Livingstone. £3·75.

Reactions to Injury and Burns and Their Clinical Importance
S. Sevitt, Birmingham. 210 × 140 mm. Pp. 255+vi. Illustrated. 1974. London: William Heinemann Medical Books. £4·25.

Lehrbuch der Chirurgie für Unterricht und Praxis in der Krankenpflege
Helmut Fass. 200 × 140 mm. Pp. 441+xviii, with 127 illustrations. 1974. Berlin: Springer-Verlag. DM.34,20.

Indikation zur Operation
Edited G. Herberer and G. Hegemann. 270 × 195 mm. Pp. 505+xvi, with 232 illustrations. 1974. Berlin: Springer-Verlag. DM.198.

Lymphatiques profonds et lymphoedemes chroniques des membres
E. Tosatti, Genes. 232 × 160 mm. Pp. 141, with 69 illustrations. 1974. Paris: Masson et Cie. 82F.

Polytraumatiqes fractures du rachis cervical. Greffon pedicule. Coaptation trochantero-iliaque. Reprises precoces. Des prostheses totales suppurées
R. Judet, Paris. 244 × 160 mm. Pp. 192+vi. Illustrated. 1974. Paris: Masson et Cie. 112F.

Head and Neck Injuries in Football. Mechanisms, Treatment and Prevention
R. C. Schneider, Michigan. 257 × 180 mm. Pp. 272+xxi. Illustrated. 1973. Baltimore: Williams & Wilkins. $18·75.

Symposium on Reconstruction of the Auricle. Volume 10
Edited Radford C. Tanzer, Vermont, and Milton T. Edgerton, Virginia. 280 × 220 mm. Pp. 312+xi, with 611 illustrations. 1974. London: Henry Kimpton. £20·20.

Atlas of Orthopaedic Surgery. Volumes 1 and 2
L. A. Goldstein and C. Dickerson, New York. 280 × 215 mm. Vol. 1: pp. 524+xiv. Vol. 2: pp. 592+xiv; 1674 illustrations. 1974. London: Henry Kimpton. £41·55.

Selected Therapeutic Problems in Rheumatoid Arthritis. Volume 6
Edited G. H. Fallet and T. L. Fischer. 240 × 165 mm. Pp. 150+viii, with 20 illustrations. 1974. München: Urban & Schwarzenberg. No price given.

Chirurgie Plastique du Sein
J.-P. Lalardrie (Paris), and J.-P. Jouglard, Marseille. 260 × 185 mm. Pp. 304, with 142 illustrations. 1974. Paris: Masson et Cie. 150F.

The Seward Identikit...

Every stainless steel Lloyd-Davies' Sigmoidoscope made by Seward has components which are absolutely identical – guaranteed interchangeable.

And that's an immense advantage when a lot of these instruments pass through the CSSD together. Because you never need to label any parts, or worry about 'matching up'.

Which saves time. Cuts losses.

You'll probably agree, the Seward Lloyd-Davies' Sigmoidoscope* is good news.

Well, here's some more.

The Seward St. Mark's Proctoscope*.

Made entirely of stainless steel. With all parts absolutely identical – guaranteed interchangeable.

**Electric and non-electric models available – leaflets on request*

seward –the fast word in quality

A. J. Seward, UAC House, Blackfriars Road, London SE1 9UG.
Telephone: 01-928 7444

PRE-WAR TOY TRAINS

Wanted for local museum Bing, Hornby and Bassett-Lowke tinplate trains—clockwork, electric or steam, including any accessories however small. Condition is not important as often one piece can be used to restore another. We are aiming to set up as complete a collection of pre-war models as possible, and welcome any relevant items. Reasonable prices paid.

P. B. WHITEHOUSE J.P., Birmingham Railway Museum, 5 Birch Hollow, Edgbaston, Birmingham B15 2QE. *Tel.:* 021 454 7395.

BRITISH JOURNAL OF SURGERY

Binding Cases

Binding cases for Volume 61 may be obtained from the Publishers at £1·25 post free. They are supplied in dark blue cloth with imitation gold lettering on the spine.

If desired, the publishers will undertake the binding at an inclusive charge of £4·00, post free.

JOHN WRIGHT

42–44 TRIANGLE WEST, BRISTOL BS8 1EX

New and Revised 11th Edition

Synopsis of Surgical Anatomy

Edited by D. J. du PLESSIS
CHM (Rand), FRCS (Eng)

Head of the Department of Surgery, University of Witwatersrand, Johannesburg; Chief Surgeon, Johannesburg General Hospital

A general revision has been undertaken to bring the whole book up to date and also to eliminate those sections which were not absolutely essential because it is important to prevent a book of this type from becoming too large. This new completely revised edition, with many excellent illustrations, is in two parts: Anatomy of the Normal and Anatomy of the Abnormal.

In preparation

About 928 pages 779 illustrations £7·00 net

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

New Surgical Titles from

CHURCHILL LIVINGSTONE

A TEXTBOOK OF SURGICAL PATHOLOGY

Sir **Charles Illingworth** and the late **Bruce M. Dick**

1975 Eleventh edition
376 pages illustrated £11·00

This volume of Surgical Pathology covers all aspects of the science of surgical diseases, including the relevant aspects of physiology and biochemistry as well as the traditional subjects of morbid anatomy and histology.

MAJOR AMPUTATIONS FOR VASCULAR DISEASE

J. M. Little

1975 128 pages illustrated £5·00

This book describes the specialised management of amputees who suffer from advanced vascular disease. There are technical descriptions of the amputations themselves and an analysis of the results that can be expected from them. The major feature is that the author adopts a 'whole patient' approach, with emphasis on the psychological adjustment to amputation.

THE INTERNAL AUDITORY MEATUS

Anatomy, Pathology and Surgery

M. Portmann, J. M. Sterkers, R. Charachon and **C. H. Chouard**

Translated by Anthony E. S. Richards

1975 318 pages illustrated £15·50

During the course of its existence as a speciality, otolaryngology has shown great capacity for change, and this has lead to the development of many new techniques which are discussed in this book.

CHURCHILL LIVINGSTONE

23 Ravelston Terrace, Edinburgh EH4 3TL

Physical Examination of the Surgical Patient:

An Introduction to Clinical Surgery 4/e

By J. Engelbert Dunphy, M.D., Professor of Surgery, University of California School of Medicine, San Francisco, California, and Thomas W. Botsford, M.D., Associate Professor of Surgery, Harvard Medical School.

This fourth edition of **Physical Examination of the Surgical Patient** has undergone extensive revision, and introduces such new emphases as the problem orientated record and pathophysiologic mechanisms of surgical disease. Major changes to this edition appear in the elective examination of the breast, heart, abdomen, and the cancer patient; the emergency examination of the chest, abdomen, and the thermally injured patient. A more clear and concise listing of supplementary readings replaces the old bibliography, and many of the older figures have been replaced with new ones. A second colour plate of epidermal lesions has also been added.

430pp 215 illustrations (2 pages in colour) Cloth binding Price £8.85
Published March 1975

Surgery in the Aged

A title in the series Major Problems in Clinical Surgery

By Lazar J. Greenfield, M.D., Professor of Surgery, The University of Oklahoma Health Sciences Centre College of Medicine, Oklahoma City, Oklahoma.

Approx 250pp Illustrated Cloth binding Approx price £6.65
Publication date September 1975

Atlas of Vaginal Surgery

By Frederick J. Hofmeister, M.D., Associate Clinical Professor, Department of Gynaecology and Obstetrics, Medical College of Winsconsin.

225pp Illustrated Cloth binding Price £8.30 Published January 1975

Surgery of the Trachea

By Hermes C. Grillo, M.D., Massachusetts General Hospital, Boston Massachusetts.

200pp Illustrated Cloth binding Price £7.75 Published January 1974

To obtain your inspection copy, write now to Colin Dann–Publicity Manager, 120 Golden Lane London EC1Y 0TU–Please quote reference WBS 9 with your reply.

W. B. Saunders Company Ltd
12 Dyott Street London WC1A 1DB

YELLOW ALERT!

When deep vein thrombosis is extending put them on Kabikinase to dissolve the clot, preserve the valves and restore the flow. (Lysis achieved, anticoagulate with heparin to prevent rethrombosis.)

KABIKINASE

(pure streptokinase)

Full information, brochure and wall card on request.

Kabikinase is manufactured by AB Kabi, Stockholm, Sweden, and is available only from:

KabiVitrum

KabiVitrum Limited,
Bilton House,
Uxbridge Road,
London W5 2TH
Telephone: 01-567 4717 01-579 1871

P. L. No. 0022/5006
Kabikinase is a registered trade mark.

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU

Trasylol

significantly reduces mortality and morbidity in acute pancreatitis

Trapnell, J. E. *et al.* (1974) *British Journal of Surgery*, **61**, 177.

Trasylol®

(aprotinin)

Bayer BAYER

® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

Vol. 62 : No. 7 : July 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
I. D. A. JOHNSTON Newcastle
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN McADAM Kampala : Uganda
A. C. McEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX

Subscription £15 per annum, post free. Single copies £1·50, post free

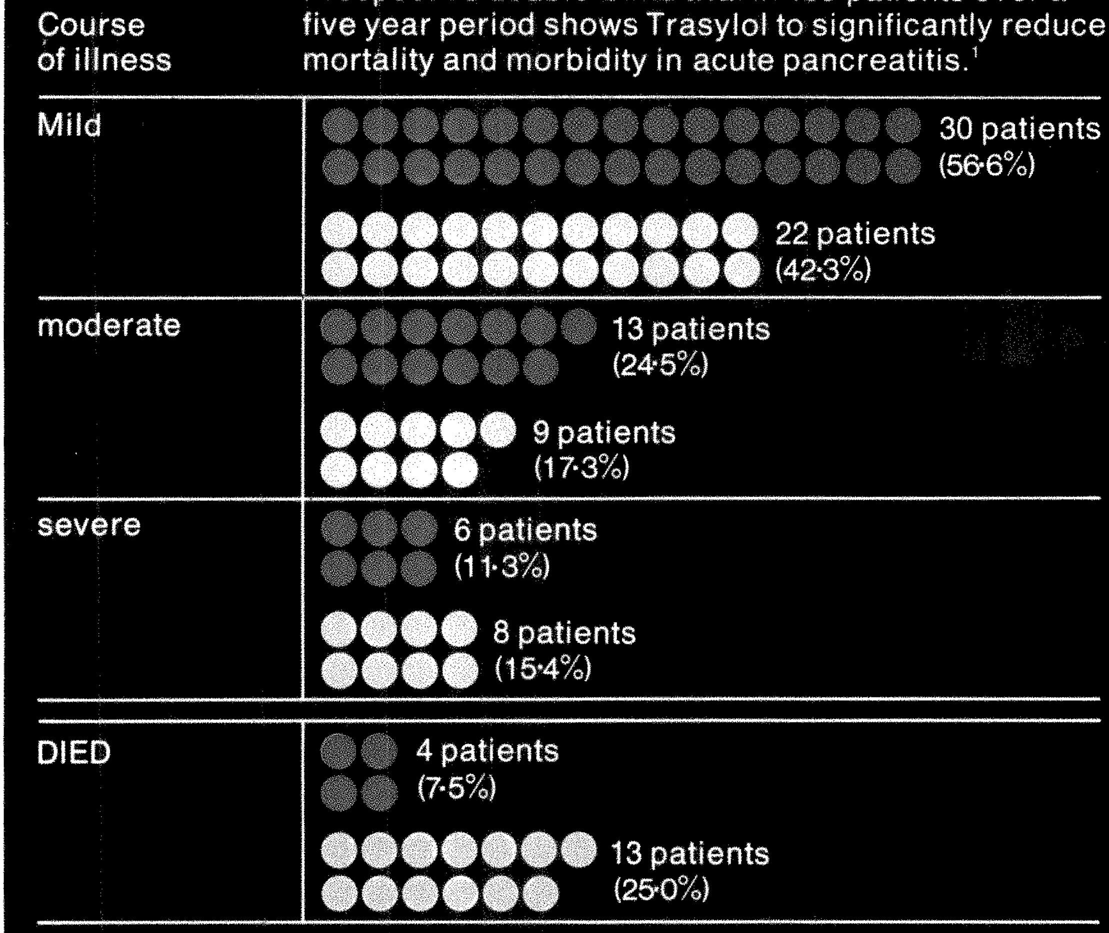
---

THE WILLIAMS & WILKINS CO., BALTIMORE

Subscription $36·00 per annum. Single copies $3·00
Second Class Postage paid at Baltimore, and at additional mailing offices.

The new evidence for Trasylol in the treatment of acute pancreatitis

Prospective double-blind trial in 105 patients over a five year period shows Trasylol to significantly reduce mortality and morbidity in acute pancreatitis.[1]



● Trasylol group (53)

○ placebo group (52)

'Trasylol must therefore be regarded as a drug which is beneficial in the treatment of acute pancreatitis.'[1]

1 Trapnell, J.E. *et al.* (1974) *British Journal of Surgery*, **61**, 177

Trasylol®

(aprotinin)

Bayer

® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

The British Journal of Surgery

Vol. 62 : No. 7 : July 1975

Page

Review paper

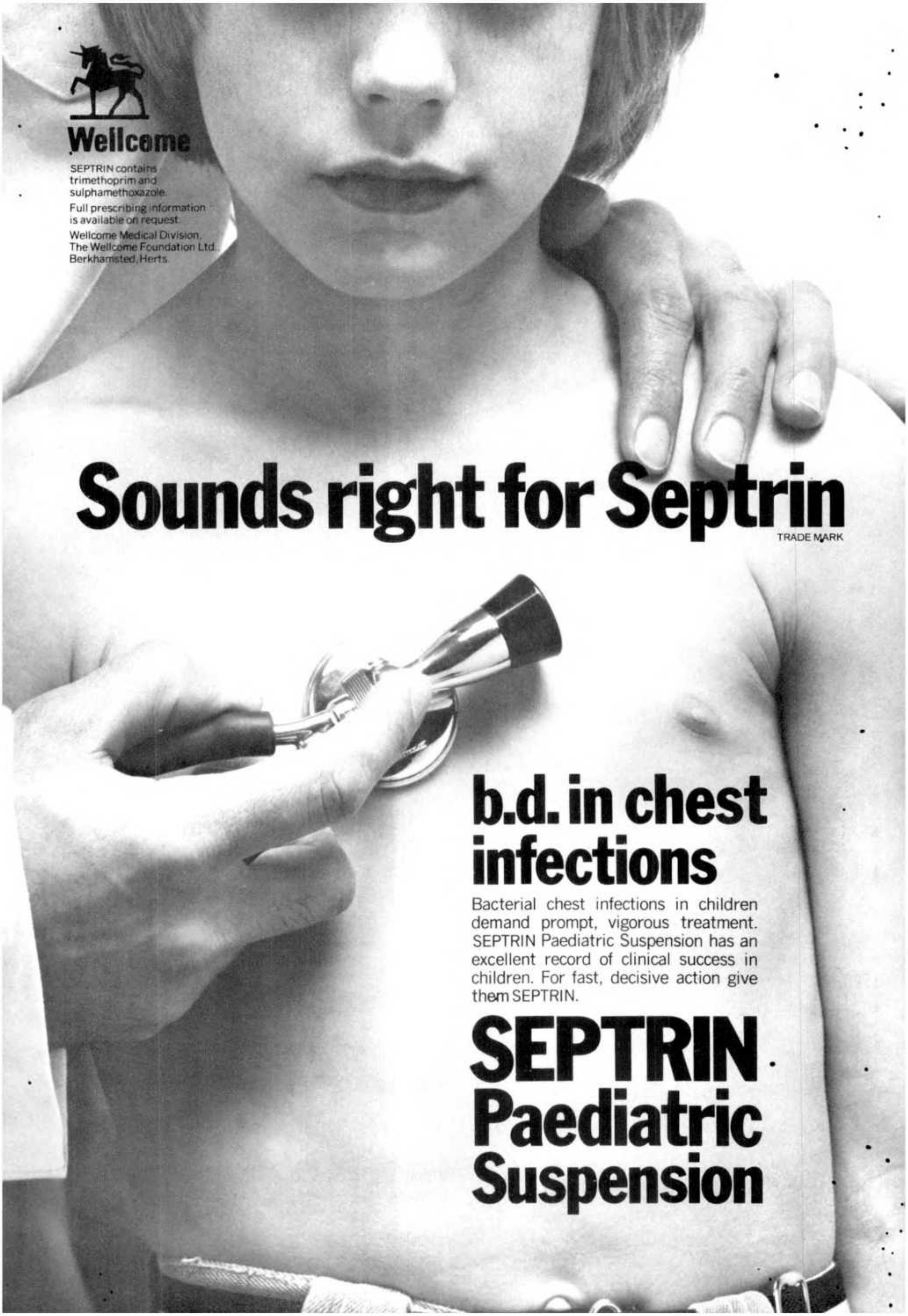
Bile salts and gallstone disease — Colin MacKay — 505

Original papers

Orthotopic liver transplantation: an experimental study on the prevention of infections with Gram-negative organisms — S. W. Schalm, D. T. Popescu, D. van der Waay, R. A. F. Krom, W. D. H. Hendriks, J. L. Terpstra and C. Jerusalem — 513
Fatal *Clostridium welchii* septicaemia following acute cholecystitis — M. T. Clancy and S. O'Briain — 518
The removal of retained gallstones from the common bile duct: experience with sodium cholate infusion and the Burhenne catheter — D. C. Britton, B. S. Gill, R. M. R. Taylor and Oliver James — 520
Long term changes in total body water, total exchangeable sodium and total body potassium before and after ileostomy — G. L. Hill, J. C. Goligher A. H. Smith and W. S. J. Mair — 524
Results of surgery for Crohn's disease in the Glasgow region, 1961–70 — S. Young, I. S. Smith, J. O'Connor, J. R. Bell and G. Gillespie — 528
Significance of faecoliths in the diagnosis of acute appendicitis — B. Gill and R. E. Cudmore — 535
The changing pattern of hospital admissions for diverticular disease of the colon — James Kyle and Alan I. Davidson — 537
The nature of haemorrhoids — W. H. F. Thomson — 542
Localization of parathyroid adenomas by computer-assisted parathyroid scanning — P. J. Ell, A. Todd-Pokropek and K. E. Britton — 553
True recurrence of hyperparathyroidism: proposed criteria of recurrence — H. Muller — 556
Recurrent pleural effusion in chronic relapsing pancreatitis — Rudra Rasaretnam, A. B. V. Perera and M. Kumarasinghe — 560
Xanthogranulomatous pyelonephritis: a report of 2 cases — O. S. Morgan, G. D. Nicholson, P. S. Johnson and D. W. Atkinson — 563
An incision for *en bloc* nephrectomy — G. F. Cassie — 565
Undetected aorto-iliac insufficiency: a reason for early failure of saphenous vein bypass grafts for obstruction of the superficial femoral artery — D. Charlesworth, P. L. Harris, F. D. Cave and Linda Taylor — 567
Ossification in extradural fat in Paget's disease of the spine — Patrick R. R. Clarke and H. I. Williams — 571
Nodular fasciitis: an unusual cause of extradural spinal cord compression — R. P. Sengupta, S. C. So and R. H. Perry — 573
Peritoneal mesothelioma — P. S. F. Chan, T. W. Balfour, J. B. Bourke and P. G. Smith — 576
The negative cholecystogram in gallbladder disease — D. R. K. Reid and I. M. Rogers — 581

Reviews and notices of books — 584

© John Wright & Sons Ltd and the respective contributors named above, 1975.
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any other form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.



Wellcome

SEPTRIN contains trimethoprim and sulphamethoxazole.

Full prescribing information is available on request.

Wellcome Medical Division,
The Wellcome Foundation Ltd.,
Berkhamsted, Herts.

b.d. in chest infections

Bacterial chest infections in children demand prompt, vigorous treatment. SEPTRIN Paediatric Suspension has an excellent record of clinical success in children. For fast, decisive action give them SEPTRIN.

SEPTRIN Paediatric Suspension

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 61. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISEMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

PRESENTATION OF STATISTICS

Authors are reminded that with the frequent use of statistical analysis in biological writing of all kinds it is desirable that:

a. The methods section of a paper should contain a mention of any statistical technique used. If the method is new or unfamiliar either a reference should be given or a description included as a brief appendix.

b. If alternative techniques could have been applied to the data, a short justification of the method is often appropriate.

c. In clinical trials the confidence or tolerance limits of the results should be quoted, particularly when formal statistical significance at the 5 per cent level is only just reached.

d. Abbreviations for statistical terms should follow those used in *Documenta Geigy Scientific Tables,* 7th edition, 1970.

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are two or more authors (apart from the main author), these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated.

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature (Lond.)* **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea **4**, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th 3d. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology*. London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BLAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

Congress Proceedings

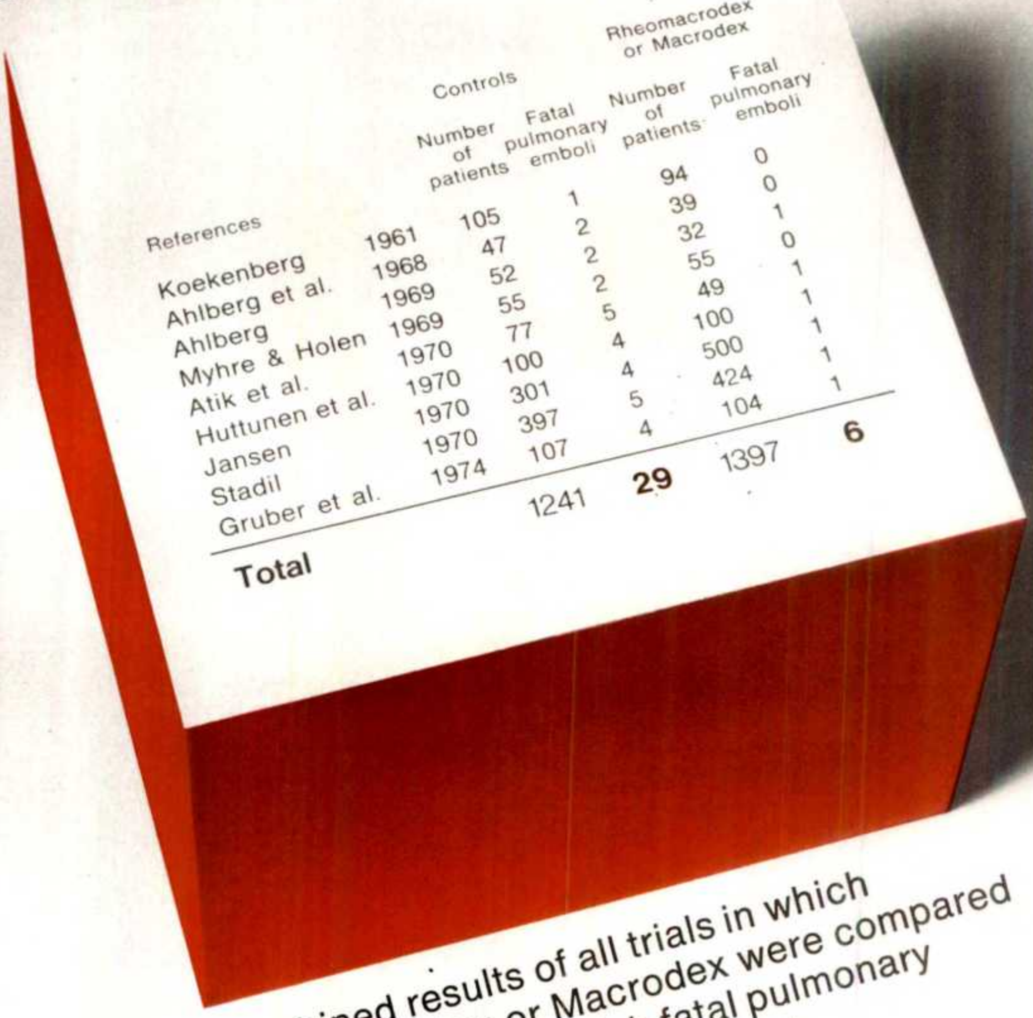
CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding, or that following.

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)

Compelling evidence mounts up: Rheomacrodex and Macrodex reduce mortality from post-operative pulmonary embolism!



References		Controls: Number of patients	Controls: Fatal pulmonary emboli	Rheomacrodex or Macrodex: Number of patients	Rheomacrodex or Macrodex: Fatal pulmonary emboli
Koekenberg	1961	105	1	94	0
Ahlberg et al.	1968	47	2	39	0
Ahlberg	1969	52	2	32	1
Myhre & Holen	1969	55	2	55	0
Atik et al.	1970	77	5	49	1
Huttunen et al.	1970	100	4	100	1
Jansen	1970	301	4	500	1
Stadil	1970	397	5	424	1
Gruber et al.	1974	107	4	104	1
Total		1241	**29**	1397	**6**

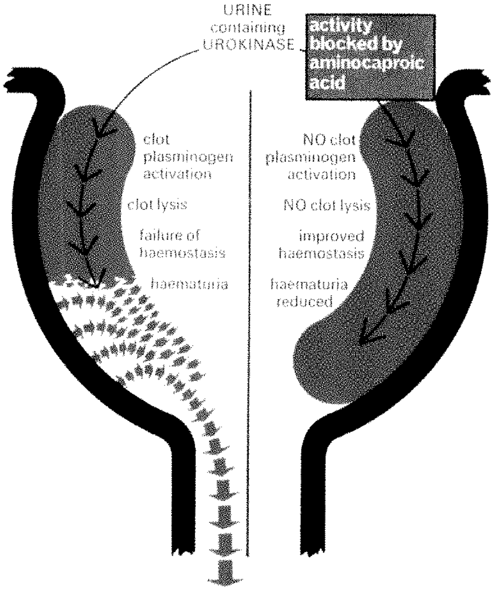
Combined results of all trials in which Rheomacrodex or Macrodex were compared to controls and in which fatal pulmonary emboli were verified by autopsy.

Pharmacia

Pharmacia (Great Britain) Limited,
Paramount House,
75 Uxbridge Road,
London W5 5SS

Rheomacrodex and Macrodex comply with the dextran 40 and 70 BP 1973 monographs respectively.

The
mechanism of
post-prostatectomy bleeding
and
EPSIKAPRON®
control



Epsikapron (aminocaproic acid) is rapidly excreted in the urine in high concentration ; there it inhibits urokinase, the fibrinolytic enzyme in urine. With the haemorrhage-sustaining property of urine blocked, the haemostatic coagulum becomes adequate, and blood loss is diminished substantially.

Epsikapron makes your prostatectomy patient's post-operative course smoother by diminishing :

the need for post-operative blood transfusion
clot retention
catheterization
the risk of infection
the period of hospitalization

Presentation

Epsikapron Solution for Injection 0.4 g/ml Box of 6 ampoules of 10 ml, each containing 4.0g aminocaproic acid (0022/5003) Epsikapron Effervescent Powder 50% Box of 30 sachets, each containing 3.0g aminocaproic acid (0022/5004) Epsikapron Syrup 0.3g/ml Bottle of 250ml (0022/5005)

EPSIKAPRON®

KabiVitrum

KabiVitrum Limited,
Bilton House,
Uxbridge Road,
London W5 2TH
Telephone: 01-567 4717 01-579 1871

The British Journal of Surgery

Vol. 62 : No. 7 : July 1975

Br. J. Surg. Vol. 62 (1975) 505–512

Bile salts and gallstone disease

COLIN MACKAY*

SUMMARY

Bile salts play an important role in maintaining cholesterol in aqueous solution in bile. There is evidence that in some patients at least gallstones arise as a result of bile salt deficiency. The evidence to date suggests that although oral bile salts may be of use in treating some gallstone patients they are unlikely to replace cholecystectomy in the foreseeable future. The instillation of bile salts via an indwelling T-tube may well be of great use in the management of stones retained in the common duct after choledocholithotomy. There is no doubt that in this branch of medicine as in all others prevention is better than cure and our aim should be to perfect our technique so that we do not leave stones behind. However, should the situation occur we may soon have safe effective physiological solvents to dissolve our mistakes.

GALLSTONE disease is a very common condition and there is evidence that it is becoming even commoner (Holland and Heaton, 1972). Although no accurate figures are available, probably about 10 per cent of the population of the United Kingdom aged over 40 years have gallstones most of which will be cholesterol in type (Sutor and Wooley, 1971). In this review three aspects will be considered: how bile salts maintain cholesterol in aqueous solution in bile, the part played by bile salts in the aetiology of gallstone disease and the role of bile salts in the treatment of gallstone disease.

Physiology

Bile salts are synthesized in the liver from cholesterol (Bergstrom and Danielsson, 1968; Mosbach, 1972), and indeed they constitute the major pathway of cholesterol excretion by the body. In man there are two primary bile acids, cholic and chenodeoxycholic, and these are excreted in bile conjugated with glycine or taurine. After entering the small bowel they pass along its length before being actively reabsorbed in the terminal ileum. This is normally a most efficient process such that some 95 per cent of bile salts are reabsorbed to return via the portal circulation to the liver and be re-excreted in bile. The bile salts in the enterohepatic circulation constitute the bile salt pool, which in man amounts to 2–4 g and recirculates two or three times during the digestion of a single meal. A small percentage of bile salts pass through the terminal ileum into the colon where they encounter bacterial enzymes. These enzymes produce deconjugation and dehydroxylation such that the glycine and taurine moieties are split off and cholate is dehydroxylated to deoxycholate and chenodeoxycholate to lithocholate. Deoxycholate is reabsorbed and returns in the portal circulation to the liver where it is conjugated with glycine or taurine and excreted in bile as a secondary bile salt. Lithocholate, on the other hand, is insoluble and is excreted in the stool so that in man only trace amounts are present in bile. Thus in human bile there are normally glycine and taurine conjugates of cholic, chenodeoxycholic and deoxycholic acids.

The principal lipids in bile in addition to the bile salts are cholesterol and phospholipid which is almost entirely lecithin. Each of these three substances is amphiphilic, i.e. part of the molecule is soluble in water and part is soluble in fat solvents. The taurine and glycine moieties of bile salts, together with the hydroxyl groups, are so strongly water soluble that they bring the whole molecule into aqueous solution and so bile salts are water soluble. However, this is not so with lecithin and cholesterol. The water soluble portions of these molecules are relatively so small that they are not strong enough to bring the rest of the molecule into aqueous solution and so lecithin and cholesterol are not soluble in water. The principal function of bile salts in bile is to maintain in aqueous solution these two substances, lecithin and cholesterol. A description of the physicochemical processes involved is beyond the scope of this article but the subject has been well reviewed by Carey and Small (1970); suffice it to say that this process of solubilization is brought about by the formation of mixed micelles—structures with a water soluble coating and a water insoluble core. In bile the bile salts form the water soluble coating and lecithin and cholesterol the water insoluble core. Lecithin, although itself insoluble in water, plays an important role in enhancing the solubility of cholesterol in bile salt micelles. Bile salt micelles are able to dissolve relatively small amounts of cholesterol, but in the presence of lecithin

---

* University Department of Surgery, Western Infirmary, Glasgow.

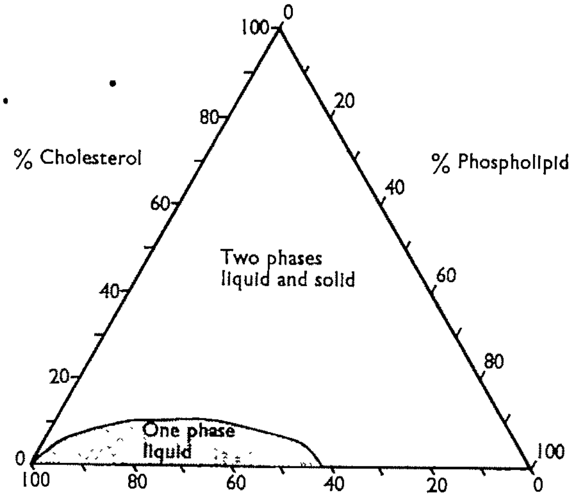


Fig. 1. Triangular coordinate plot showing physicochemical characteristics of solutions containing different proportions of bile salt, cholesterol and lecithin.

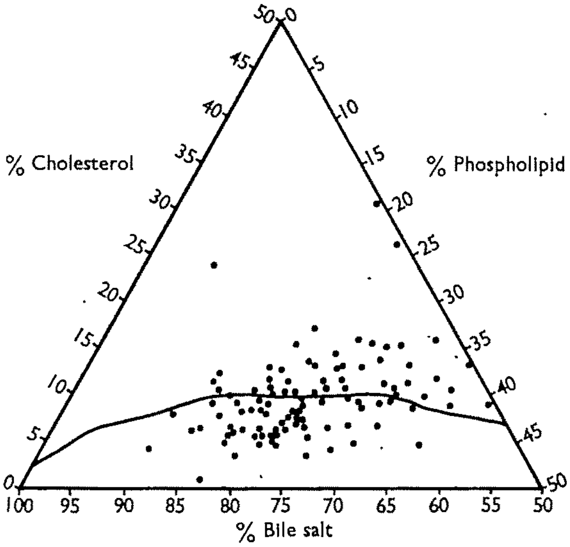


Fig. 2. Relative composition of hepatic bile obtained at the time of cholecystectomy from 103 gallstone patients.

the micelle is expanded and the cholesterol solubility enhanced.

In the small intestine bile salts play an important role in the digestion and absorption of fat. They aid in the emulsification of fat, help activate pancreatic lipase and render water soluble the products of pancreatic lipolysis. Pancreatic lipase hydrolyses triglyceride into monoglyceride and fatty acid, substances which are insoluble in water but which are rendered water soluble by the formation of mixed micelles with bile salts. Bile salts are similarly involved in the absorption of the fat soluble vitamins.

Bile salts and aetiology of gallstones

We have established the role of bile salts in maintaining cholesterol in aqueous solution in bile. This process was further elucidated by Admirand and Small (1968), who constructed an *in vitro* model system which allowed the prediction of the maximum amount of cholesterol which could be dissolved in aqueous solutions containing varying proportions of bile salt and lecithin. They expressed their results on triangular coordinates and constructed a phase diagram as shown in *Fig*. 1. All mixtures whose relative composition lay within the shaded area were in micellar solution whereas all others contained crystals of cholesterol. They then studied the relative amounts of bile salt, cholesterol and phospholipid in gallbladder bile from patients with cholesterol gallstones and in bile from patients without gallstones. They showed that normal bile was less than saturated with cholesterol relative to bile salt and phospholipid whereas bile from patients with cholesterol gallstones was saturated and in some cases contained insoluble cholesterol in the form of microcrystals. As a result of these studies they suggested that the physical state of bile (i.e. the presence or absence of insoluble cholesterol) was determined by the relative concentration of bile salt, lecithin and cholesterol.

There is no doubt that this was a major advance in the understanding of the aetiology of gallstones, but it is important to emphasize that they established the limits of cholesterol solubility from *in vitro* studies and that only one bile salt, sodium taurocholate, was studied. Whether or not their findings apply *in vivo* and are applicable for all bile salts remains to be shown and this should be borne in mind when their findings are applied to the clinical situation. They themselves showed that alteration of the total solids outwith the range of 5–20 per cent altered the line of maximum solubility of cholesterol in bile salt and lecithin, and it may well be that other factors, as yet unknown, also alter the limits of solubility. With these reservations, however, it would appear, from the studies of Admirand and Small, that cholesterol gallstones are associated with gallbladder bile which is saturated with cholesterol.

Is this bile secreted in a saturated form by the liver or does it become saturated in the gallbladder? Almost simultaneously Small and Rapo (1970) and Vlahcevic et al. (1970b) reported studies in which they examined the relative composition of gallbladder bile and hepatic bile in patients undergoing cholecystectomy for cholesterol gallstones. Both groups showed that hepatic bile was supersaturated with cholesterol and the conclusion was reached that cholesterol gallstones were due to the production by the liver, and not the gallbladder, of abnormal bile. Since these two studies were reported, others studying the relative composition of bile at the time of cholecystectomy have shown that while many patients with cholesterol gallstones secrete supersaturated hepatic bile this is not always the case, as shown by MacKay et al. (1972), Smallwood et al. (1972) and Heller and Bouchier (1973). The latest data of the author are shown in *Fig*. 2, from which it is evident that although many patients with cholesterol gallstones do secrete hepatic bile which is supersaturated with cholesterol, a large number secrete bile whose relative composition lies within the micellar zone. Studies of bile composition in gallstone patients are open to the criticism that they give no indication of the composition of bile pertaining at the time of initiation of stone formation, and it is entirely possible that patients with a bile which is not supersaturated at the time of cholecystectomy could well have secreted supersaturated bile at some time in the past. The finding of undersaturated bile at the time of cholecystectomy does not therefore preclude the part played by supersaturation of bile in the initiation of gallstone formation.

Supersaturated bile came to be known as 'lithogenic', but care should be exercised in the use of this term. Nakayama and Van der Linden (1970) showed that many patients without gallstones secreted supersaturated bile, and Metzger et al. (1973) showed that fasting bile was consistently more 'lithogenic' than gallbladder bile or hepatic bile obtained during feeding and this occurred even in patients without gallstones. Metzger's findings were supported by Northfield and Hofmann (1973), who showed that the secretion of 'lithogenic' bile occurred with equal frequency in gallstone patients and controls, especially during overnight fasting, and seemed to be physiological. It may be that the production of supersaturated bile during fasting, if prolonged or combined with inadequate mixing within the gallbladder, could be an important factor in the formation of cholesterol gallstones.

The association of cholesterol gallstones with supersaturation of bile gains support from some epidemiological and animal studies. Redinger and Small (1972) have collected data showing that there is a correlation between the prevalence of gallstone disease and the degree of saturation of gallbladder bile in different ethnic groups. From *Fig.* 3 it is evident that young North American Indian females who have a high prevalence of cholesterol gallstones also have a high percentage of cholesterol saturation in bile, whereas the African Masai, a population in which cholesterol gallstones do not occur, have a much lower percentage saturation. These workers also cited data from animal studies showing that animals which do not form gallstones spontaneously and only with difficulty by dietary manipulation, e.g. dog and pig, secrete bile containing little cholesterol relative to bile salt and phospholipid. Hamsters, on the other hand, secrete bile with a relatively higher proportion of cholesterol and although they do not form stones spontaneously they can be induced to do so fairly readily by dietary manipulation. Baboons secrete bile which has a relative composition approaching the limits of cholesterol solubility and they are known to form stones spontaneously without dietary manipulation. These data are illustrated in *Fig.* 4.

How can the current state of knowledge be summarized? It would appear that in many patients with cholesterol gallstones hepatic bile contains an excess of cholesterol relative to bile salt and phospholipid, and even in the others the bile may well have been supersaturated at some time in the past. In view of the fact that bile is 'normally' supersaturated when patients are fasting it is perhaps not surprising that some patients develop gallstones but more surprising that all patients do not develop a stone. It should be emphasized that supersaturation is only one event in the formation of a gallstone; it has to be followed by the precipitation of cholesterol and the formation of microstones which enlarge to form macrostones (Small, 1970). It may well be that in patients who do not develop gallstones precipitation does not occur or should it occur the crystals are washed out in the bile into the gastro-intestinal tract.

We have established the role of supersaturation of hepatic bile in the aetiology of cholesterol gallstones.

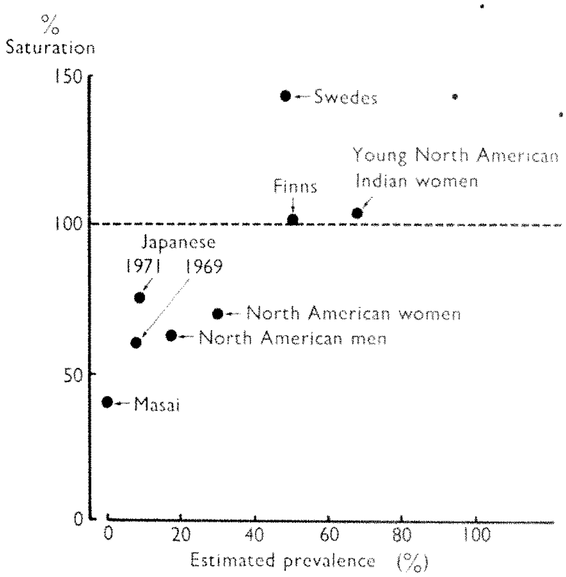


Fig. 3. Percentage cholesterol saturation of gallbladder bile in different populations (from the data of Redinger and Small, 1972, as adapted by Lukie and Dietschy, 1973).

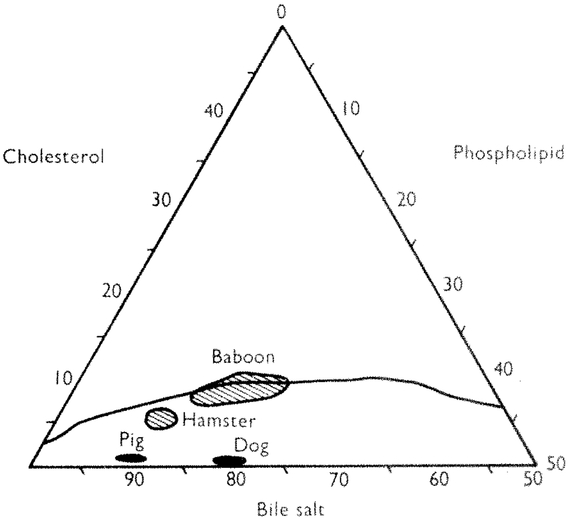


Fig. 4. Relative composition of animal gallbladder bile (adapted from Redinger and Small, 1972).

Theoretically, this could arise from excessive cholesterol secretion or impaired bile salt and/or phospholipid secretion. There is some evidence to suggest that cholesterol intake may influence bile composition but little evidence to incriminate phospholipid. These subjects are beyond the scope of this article which considers the evidence that cholesterol gallstones are due to a lack of bile salts. It is possible to measure the size of the bile salt pool in man by administering bile salt labelled with a radioactive isotope and aspirating specimens of bile by duodenal intubation. Vlahcevic et al. (1970a) measured the pool size by this method of isotope dilution; they gave ^{14}C cholic acid to gallstone patients and controls and found that the pool size was significantly smaller in the gallstone patients. Arnesjö and Stahl (1973) and Danzinger et al. (1973) also reported a reduced bile acid pool size in gallstone patients. However, it could be argued that the diminished pool size was the result rather than the cause of the gallstones. The studies of Bell et al. (1973) would suggest that the diminished pool size was more likely to precede than to result from the gallstones. They studied bile salt pool size in three groups of American Indians, namely: (*a*) patients with gallstones and saturated bile; (*b*) patients without gallstones but saturated bile; (*c*) patients with no gallstones and normal bile. The pool size was greatly diminished in both groups of saturated bile patients. The fact that the pool was reduced even in the patients with no evidence of gallstones would suggest that the reduced pool preceded rather than resulted from the gallstones. Care must be taken in drawing too many conclusions from studies in American Indians with their remarkably high prevalence of gallstone disease (Sampliner et al., 1970), as the aetiology in such patients may be very different from the aetiology in other populations with a much lower prevalence of gallstone disease.

The hypothesis that a diminished bile acid pool size is responsible for the production of cholesterol gallstones received further support from the work of Heaton and Read (1969). They studied the prevalence of gallstones in patients who had previously undergone resection of the terminal ileum, the bile-salt-absorbing area of the gut, and found the prevalence to be significantly higher than in control groups. Abaurre et al. (1969) have shown that patients with ileal resection have a diminished bile salt pool.

It has been assumed that this small bile acid pool recirculates at the normal rate in the enterohepatic circulation, thus leading to a reduced secretion rate of bile acid but not cholesterol in bile. Northfield and Hofmann (1973) studied biliary lipid output in patients with radiolucent gallstones and in matched controls. They found that there was an inverse relationship between the size and the recycling rate of the bile salt pool so that the bile salt secretion rate remained constant over a wide range of pool sizes. They found that the total daily output of all three biliary lipids was similar in gallstone patients and controls. This is in contrast to the findings of Grundy et al. (1972), who showed that obese American Indian women with gallstones had a higher cholesterol output and a lower bile salt output than thin Caucasian controls, the diminished bile salt output probably arising from impaired hepatic synthesis. This difference may well be racial, the American Indians having a much higher prevalence of gallstone disease. Low-Beer and Pomare (1973) also showed that the size of the bile salt pool was largely determined by the frequency of its enterohepatic circulation. Therefore the exact role of a small bile acid pool in the pathogenesis of cholesterol gallstones remains to be determined.

The part played by a reduced bile salt pool in the production of cholesterol gallstones has been considered, but is there any evidence that an alteration in its component bile salts is responsible for gallstone formation? Van der Linden (1971) has reviewed the available literature and shown that there is a tendency for patients with gallstones to have an increase in dihydroxy bile salts relative to trihydroxy salts. He pointed out that while the difference did not reach the level of statistical significance in many of the studies reported the regular trend could not be ignored. The ratio of trihydroxy to dihydroxy bile salts in gallstone and duodenal ulcer patients studied by the author was found to be 0·44 and 0·67 respectively, the difference being statistically significant. Similar findings have been reported by Arnesjö and Stahl (1973) and Heller and Bouchier (1973). There would seem, therefore, to be good evidence that gallstones are associated with a relative increase in dihydroxy or a relative decrease in trihydroxy bile salts. Dihydroxy bile acids have been claimed to form larger micelles with less surface charge and consequently less stability (Bouchier and Freston, 1968), and a shift towards these acids may therefore favour gallstone formation. Haslewood (1967) has suggested that man's liability to gallstones may be connected with the fact that while having a herbivore's bile acid pattern, i.e. mainly dihydroxycholanic acids, he eats to a great extent a carvinore's diet and carnivores have predominantly cholic acid. The ratio of glycine-conjugated to taurine-conjugated bile salts in gallstone and duodenal ulcer patients studied by the author was found to be 2·4 and 2·1 respectively, the difference not reaching a level of statistical significance. Similar findings were reported by Arnesjö and Stahl (1973). Alterations in the patterns of conjugation cannot therefore be incriminated.

A few years ago it seemed as if the gallstone problem had been solved, the cause being a hepatic abnormality resulting in the production of bile supersaturated with cholesterol. Since then further data have complicated rather than simplified the problem, and recently the gallbladder has again been implicated. In the past stasis and infection in the gallbladder were blamed with little good scientific evidence. Dilatation of the gallbladder occurs in the later stages of pregnancy (Gerdes and Boyden, 1938), in the progesterone phase of the menstrual cycle (Nilsson and Stattin, 1967) and after truncal vagotomy (Rudick and Hutchison, 1964; Parkin et al., 1973). Gallstones are commoner in females than in males, certainly in the childbearing age groups, and may be commoner in patients after vagotomy, although this is a matter for debate (Fletcher and Clark, 1968). Impaired gallbladder emptying with stasis of bile and particularly bile salts may lead to a functional diversion of bile salts from the enterohepatic circulation and a tendency, therefore, for hepatic bile to become temporarily supersaturated, with the risk of cholesterol precipitation. The whole question of the role of the gallbladder in the aetiology of gallstones requires further investigation, especially since it has been shown that hepatic bile which was supersaturated prior to cholecystectomy tends to become normal after removal of the gallbladder (Shaffer et al., 1972; Simmons et al., 1972; Smith et al., 1973).

Bile salts and the treatment of gallstone disease

Thistle and Schoenfield (1971) at the Mayo Clinic were the first to show that the oral adminstration of chenodeoxycholic acid to women with gallstones produced a significant increase in the ratio of cholesterol-solubilizing agents in bile to cholesterol, i.e. the 'lithogenic' potential of bile was decreased. This group then went on to show (Danzinger et al., 1972) that chenodeoxycholic acid not only improved the relative composition of bile by expanding the diminished bile salt pool but caused stones to decrease in size and even disappear in some patients. These results were confirmed in this country by Bell, Whitney and Dowling (1972). The next step was to establish a trial, and the initial results of a single blind controlled therapeutic trial have been reported from the Mayo Clinic by Thistle and Hofmann (1973). They studied 53 patients with asymptomatic radiolucent gallstones in functioning gallbladders. The patients received chenodeoxycholic acid, cholic acid or a placebo. After 6 months 11 of 18 patients receiving chenodeoxycholic acid showed a decrease in gallstone size or number, but no response was observed in the 17 treated with cholic acid or in the 18 receiving a placebo. Since then a multicentre investigation into the efficacy and safety of chenodeoxycholic acid has been initiated in the United States of America supported by the National Institutes of Health (Schoenfield, 1974).

There is therefore no doubt that chenodeoxycholic acid is effective in treating some patients with gallstones but many questions remain to be answered:

1. What is the optimum dose?
2. What are the side effects of treatment?
3. Is long term treatment safe?
4. Why is chenodeoxycholic acid effective and cholic acid ineffective?
5. Is chenodeoxycholic acid the best bile acid?
6. Has treatment to continue for life?
7. Does the calcium content of the stone affect its rate of dissolution?
8. What are the contraindications to treatment?

1. *Dosage*

The dosage of chenodeoxycholic acid used in the early studies ranged from 1·5 to 4·5 g/day but this has been reduced in later studies. In the Mayo Clinic trial the dose varied from 10 to 26 mg/kg body weight. The lowest therapeutic dose remains to be determined.

2. *Side effects*

One of the potentially most troublesome side effects is diarrhoea due to the secretion of water and electrolytes by the colonic mucosa. This is dose related, and in the controlled trial reported by Thistle and Hofmann (1973) patients adjusted the dose so that the stools were usually partially or completely formed. Symptoms of gastric irritation have not occurred to any great extent in the studies reported.

3. *Safety of long term treatment*

The main worries over long term treatment are liver damage and the development of atheroma. Chenodeoxycholic acid may induce liver damage directly or via its bacterial metabolite lithocholic acid. Transient elevation of the serum transaminases during treatment has been reported (Thistle and Hofmann, 1973). Bell et al. (1974) studied liver biopsies from patients receiving chenodeoxycholic acid (0·5–1·5 g/day) and from patients with untreated cholelithiasis and found no appreciable difference; they considered that in this dosage chenodeoxycholic acid was not hepatotoxic.

There are several reasons, albeit theoretical, why the long term administration of bile salt might lead to cholesterol retention by the body and the risk of atheroma. First, the administration of exogenous bile salt will inhibit endogenous bile salt synthesis, thus abolishing one of the major excretory routes for cholesterol. Secondly, exogenous bile salt may well enhance the intestinal absorption of dietary and endogenous cholesterol. Thirdly, since bile salts alter the relative composition of bile in such a way that there is a smaller percentage of cholesterol, unless a marked increase in bile secretion occurred the total secretion of cholesterol into the intestine would be depressed (Small, 1971). These theoretical considerations were put to the test by Hoffman et al. (1974). They measured the cholesterol pool and the cholesterol input to the pool in 23 patients with gallstones; 8 receiving chenodeoxycholic acid, 7 receiving cholic acid and 8 receiving a placebo. The values were similar in all three groups and were almost the same as those reported for patients without gallstones. They concluded that chenodeoxycholic acid did not cause any major change in the body's cholesterol metabolism and that the likelihood of detectable acceleration of atheroma was quite small. They admitted, however, that any increase in cholesterol pool size may have been too small to be detectable by presently available methods. In addition, bile salts were given for a period of 6 months and the effect of more prolonged administration is unknown. It may well be that patients with hyperlipidaemia, atheroma or a tendency to develop atheroma behave in a different way; these patients may have difficulty in excreting cholesterol and the additional strain imposed by bile salt adminstration may further exacerbate cholesterol handling. Further work is required before chenodeoxycholic acid can be completely cleared of the charge of being potentially atherogenic.

4. *Mechanism of action*

The precise mechanism by which chenodeoxycholic acid alters the composition of bile and produces gallstone dissolution is not clear. It cannot simply be due to an increase in the size of the bile salt pool because cholic acid also increases the bile salt pool size and yet does not alter the relative composition of bile or dissolve gallstones. Recent measurements of biliary lipid secretion before and after ingestion of chenodeoxycholic acid suggest that its major effect is to cause a relative or absolute reduction in cholesterol secretion (Northfield et al., 1973). Salen et al. (1973) have reported data suggesting that chenodeoxycholic acid reduced the activity of HMG-CoA reductase, an enzyme which regulates cholesterol synthesis by the liver. Confirmation of these findings is awaited.

5. *Best bile acid*

To date chenodeoxycholic acid is the best available. Farrell et al. (1973) have shown by *in vitro* studies of gallstone dissolution that dihydroxy bile salts are more efficient than trihydroxy bile salts and glycine conjugates more efficient than taurine conjugates. It may well be that further work will produce a more effective bile salt or even a better synthetic detergent.

6. *Length of treatment*

The natural history of patients whose gallstones have been dissolved medically is unknown, but it would seem that the relative composition of bile returns to pre-treatment values within 1 month of stopping treatment. Gallstones recurred in 2 of the first 5 patients in whom therapy was discontinued for 1 year. It may well be that even after successful stone dissolution continuous or intermittent prophylactic therapy will be necessary (Schoenfield, 1974).

7. *Effect of calcium content of stone*

Bell, Sutor et al. (1972) showed from *in vitro* studies that an outer ring of calcification delayed gallstone dissolution. In Thistle and Hofmann's (1973) trial of 13 patients with radio-opaque gallstones, 11 showed no change in stone size or number in response to chenodeoxycholic acid, presumably because the calcium prevented the bile salt from gaining access to the cholesterol.

8. *Contraindications*

There would seem to be no point in treating patients with blockage of the cystic duct as the bile salt would not enter the gallbladder to dissolve the stones. Similarly, treatment is contraindicated in patients with a high calcium content of the stones, as bile salt, although entering the gallbladder, would be unable to dissolve the stones. However, it remains to be shown how accurate an estimate of stone calcium can be made from inspection of a radiograph.

The safety of treatment in pregnancy and inflammatory bowel disease is quite unknown.

How can we summarize the current position of chenodeoxycholic acid in the treatment of cholesterol gallstones? There is no doubt that stones can be dissolved, but the place of this therapy in the management of the condition as a whole requires much more investigation and should at the moment be considered to be at the research and development stage. The words of Kurt Isselbacher (1972) are still true: 'In the meantime our surgical colleagues can relax, their treatment of gallstones, although threatened, is not yet out-moded.'

Does this mean that bile salts have no place in the surgeon's armamentarium? There may well be an important use for bile salts in the management of the stone retained in the common bile duct following choledocholithotomy. While no surgeon will admit to seeing this condition frequently, it is surprising how often such cases are referred from that mythical 'other hospital'. These patients are often frail and poor surgical risks and the retained stone is frequently small, otherwise it would not have been missed in the first place. Most of us have at some time or another spent time and sweat looking for a stone which was blatantly obvious in the T-tube cholangiogram but not nearly so obvious at the second operation. For these reasons it would be useful to have a safe effective gallstone solvent which could be introduced via the indwelling T-tube. Do bile salts come into this category?

Way et al. (1972) reported results from 22 patients with residual stones in the common bile duct who had a sodium cholate solution infused via an indwelling T-tube. Stones were eliminated in 12 patients while the treatment was unsuccessful in the remaining 10. Lansford et al. (1974) reported success in 5 of 6 patients treated in a similar fashion. The solution is sterilized by Millipore filtration and is given by gravity drip in such a way that excessive pressure rises within the common duct are avoided. Diarrhoea almost always arises owing to the cathartic action of the bile salt, but this can usually be controlled with cholestyramine.

Although preliminary experience with this method of treatment is promising it must be stated that it has not been subjected to a controlled trial. In addition, postoperative cholangiograms can be difficult to interpret and all filling defects are not stones. For this reason more than one cholangiogram should be performed before using bile salt infusion. It is difficult to be sure how sodium cholate exerts its beneficial effect—how much is due to cholesterol solubilization and how much to mechanical flushing. Catt et al. (1974) have shown that simply infusing saline was successful in 6 out of 10 patients. Farrell et al. (1973) have found from *in vitro* studies that trihydroxy bile salts such as sodium cholate are less effective than dihydroxy bile salts at dissolving gallstones. However, it may be unnecessary to dissolve the stone completely; simply reducing it to a size at which it starts to disintegrate or is small enough to negotiate the ampulla of Vater may be sufficient.

Gardner (1973) has reported stone disappearance following the infusion of heparinized saline, and the combined use of heparin and bile salts merits further investigation.

References

ABAURRE R., GORDON S. G., MANN J. G. and KERN F. (1969) Fasting bile salt pool size and composition after ileal resection. *Gastroenterology* **57**, 679–688.

ADMIRAND W. H. and SMALL D. M. (1968) The physicochemical basis of cholesterol gallstone formation in man. *J. Clin. Invest.* **47**, 1043–1052.

ARNESJÖ B. and STAHL E. (1973) Taurocholate metabolism in patients with cholesterol gallstones. *Scand J. Gastroenterol.* **8**, 369–375.

BELL C. C. jun., VLAHCEVIC L. R., PRAZICH J. and SWELL L. (1973) Evidence that a diminished bile acid pool precedes the formation of cholesterol gallstones in man. *Surg. Gynecol. Obstet.* **136**, 961–965.

BELL G. D., MOK H. Y. I., THWE M., MURPHY G. M., HENRY K. B. and DOWLING R. H. (1974) Liver structure and function in cholelithiasis: effect of chenodeoxycholic acid. *Gut* **15**, 165–172.

BELL G. D., SUTOR D. J. WHITNEY B. and DOWLING R. H. (1972) Factors influencing human gallstone dissolution in monkey, dog and human bile. *Gut* **13**, 836.

BELL G. D., WHITNEY B. and DOWLING R. H. (1972) Gallstone dissolution in man using chenodeoxycholic acid. *Lancet* **2**, 1213–1216.

BERGSTROM S. and DANIELSSON H. (1968) The formation and metabolism of bile acids. In: CODE C. F. and HEIDEL B. (ed.) *Handbook of Physiology*, Section 6, Vol. V. Washington DC, American Physiological Society, pp. 2391–2408.

BOUCHIER I. A. D. and FRESTON J. W. (1968) The aetiology of gallstones. *Lancet* **1**, 340–349.

CAREY M. C. and SMALL D. M. (1970) The characteristics of mixed micellar solutions with particular reference to bile. *Am. J. Med.* **49**, 590–608.

CATT P., HOGG F., CLUNIE G. and HARDIE I. (1974) Retained biliary calculi: removal by a simple non-operative technique. *Ann. Surg.* **180**, 247–251.

DANZINGER R. G., HOFMANN A. F., SCHOENFIELD L. J. and THISTLE J. L. (1972) Dissolution of cholesterol gallstones by chenodeoxycholic acid. *New Engl. J. Med.* **286**, 1–8.

DANZINGER R. G., HOFMANN A. F., THISTLE J. L. and SCHOENFIELD L. J. (1973) Effect of oral chenodeoxycholic acid on bile acid kinetics and biliary lipid composition in women with cholelithiasis. *J. Clin. Invest.* **52**, 2809–2821.

FARRELL K. E., SMITH D. C. and MACKAY C. (1973) Gallstone dissolution *in vitro*. *Br. J. Surg.* **60**, 900.

FLETCHER D. M. and CLARK C. G. (1968) Gallstones and gastric surgery. *Br. J. Surg.* **55**, 895–899.

GARDNER B. (1973) Experiments with the use of intracholedochal heparinised saline for the treatment of retained common duct stones. *Ann. Surg.* **177**, 240–244.

GERDES M. M. and BOYDEN E. A. (1938) The rate of emptying of the human gallbladder in pregnancy. *Surg. Gynecol. Obstet.* **66**, 145–156.

GRUNDY S. M., METZGER A. L. and ADLER R. (1972) Defective bile salt synthesis as cause of cholesterol gallstones. *J. Clin. Invest.* **51**, 3026–3043.

HASLEWOOD G. A. D. (1967) *Bile Salts.* London, Methuen, p. 69.

HEATON K. W. and READ A. E. (1969) Gallstones in patients with disorders of the terminal ileum and disturbed bile salt metabolism. *Br. Med. J.* **3**, 494–496.

HELLER F. and BOUCHIER I. A. D. (1973) Cholesterol and bile salt studies on the bile of patients with cholesterol gallstones. *Gut* **14** 83–88.

HOFFMAN N. E. HOFMANN A. F. and THISTLE J. L. (1974) Effect of bile acid feeding on cholesterol metabolism in gallstone patients. *Mayo Clin. Proc.* **49**, 236–239.

HOLLAND C. and HEATON K. W. (1972) Increasing frequency of gallbladder operations in the Bristol clinical area. *Br. Med. J.* **3**, 672–675.

ISSELBACHER K. J. (1972) A medical treatment for gallstones? *New Engl. J. Med.* **286**, 40–42.

LANSFORD C., MEHTA S. and KERN F. (1974) The treatment of retained stones in the common bile duct with sodium cholate infusion. *Gut* **15**, 48–51.

LOW-BEER T. S. and POMARE E. W. (1973) Regulation of bile salt pool size in man. *Br. Med. J.* **1**, 338–340.

LUKIE B. E. and DIETSCHY J. M. (1973) Cholesterol gallstone formation: recent advances in pathophysiology. *Tex. Med.* **69**, 90–100.

MACKAY C., CROOK J. N., SMITH D. C. and MCALLISTER R. A. (1972) The composition of hepatic and gallbladder bile in patients with gallstones. *Gut* **13**, 759–762.

METZGER A. L., ADLER R., HEYMSFIELD S. and GRUNDY S. M. (1973) Diurnal variation in biliary lipid composition. Possible role in cholesterol gallstone formation. *New Engl. J. Med.* **288**, 333–336.

MOSBACH E. H. (1972) Hepatic synthesis of bile acids. Biochemical steps and mechanisms of rate control. *Arch. Intern. Med.* **130**, 478–487.

NAKAYAMA F. and VAN DER LINDEN W. (1970) Bile from gallbladder harbouring gallstone: can it indicate stone formation? *Acta Chir. Scand.* **136**, 605–610.

NILSSON S. and STATTIN S. (1967) Gallbladder emptying during the normal menstrual cycle. *Acta Chir. Scand.* **133**, 648–652.

NORTHFIELD T. C. and HOFMANN A. F. (1973) Biliary lipid secretion in gallstone patients. *Lancet.* **1**, 747–748.

NORTHFIELD T. C., LA RUSSO N. F., THISTLE J. L. and HOFMANN A. F. (1973) Effect of chenodeoxycholic acid therapy on biliary lipid secretion in gallstone patients. *Gastroenterology* **64**, 780.

PARKIN G. J. S., SMITH R. B. and JOHNSTON D. (1973) Gallbladder volume and contractility after truncal, selective and highly selective (parietal-cell) vagotomy in man. *Ann. Surg.* **178**, 581–586.

REDINGER R. N. and SMALL D. M. (1972) Bile composition, bile salt metabolism and gallstones. *Arch. Intern. Med.* **130**, 618–630.

RUDICK J. and HUTCHISON J. S. F. (1964) Effects of vagal-nerve section on the biliary system. *Lancet* **1**, 579–581.

SALEN G., NICOLAU G. and SHEFER S. (1973) Chenodeoxycholic acid (CDCA) inhibits elevated hepatic HMG-CoA reductase activity in subjects with gallstones. *Clin. Res.* **21**, 523.

SAMPLINER R. E., BENNETT P. M., COMESS L. J., ROSE F. A. and BURCH T. A. (1970) Gallbladder disease in Pima Indians. Demonstration of high prevalence and early onset by cholecystography. *New Engl. J. Med.* **283**, 1358–1364.

SCHOENFIELD L. J. (1974) Medical therapy for gallstones. *Gastroenterology* **67**, 725–729.

SHAFFER E. A., BRAASCH J. W. and SMALL D. M. (1972) Bile composition at and after surgery in normal persons and patients with gallstones. Influence of cholecystectomy. *New Engl. J. Med.* **287**, 1317–1322.

SIMMONS F., ROSS A. P. J. and BOUCHIER I. A. D. (1972) Alterations in hepatic bile composition after cholecystectomy. *Gastroenterology* **63**, 466–470.

SMALL D. M. (1970) The formation of gallstones. *Adv. Intern. Med.* **16**, 243–264.

SMALL D. M. (1971) Prestone gallstone disease—is therapy safe? *New Engl. J. Med.* **284**, 214–216.

SMALL D. M. and RAPO S. (1970) Source of abnormal bile in patients with cholesterol gallstones. *New Engl. J. Med.* **283**, 53–57.

SMALLWOOD R. A., JABLONSKI P. and WATTS J. MCK. (1972) Intermittent secretion of abnormal bile in patients with cholesterol gallstones. *Br. Med. J.* **4**, 263–266.

SMITH D. C., MCALLISTER R. A. and MACKAY C. (1973) The effect of cholecystectomy on the composition of bile in gallstone patients. *Br. J. Surg.* **60**, 899.

SUTOR D. J. and WOOLEY S. E. (1971) A statistical survey of the composition of gallstones in eight countries. *Gut* **12**, 55–64.

THISTLE J. L. and HOFMANN A. F. (1973) Efficacy and specificity of chenodeoxycholic acid therapy for dissolving gallstones. *New Engl. J. Med.* **289**, 655–659.

THISTLE J. L. and SCHOENFIELD L. J. (1971) Induced alterations in composition of bile of persons having cholelithiasis. *Gastroenterology* **61**, 488–496.

VAN DER LINDEN W. (1971) Bile acid pattern of patients with and without gallstones. *Gastroenterology* **60**, 1144–1145.

VLAHCEVIC Z. R., COOPER-BELL C., BUHAC I., FARRAR J. T. and SWELL L. (1970a) Diminished bile acid pool size in patients with gallstones. *Gastroenterology* **59**, 165–173.

VLAHCEVIC Z. R., COOPER-BELL C. and SWELL L. (1970b) Significance of the liver in the production of lithogenic bile in man. *Gastroenterology* **59**, 62–69.

WAY L. W., ARMIRAND W. H. and DUNPHY J. E. (1972) Management of choledocholithiasis. *Ann. Surg.* **176**, 347–359.

Br. J. Surg. Vol. 62 (1975) 513–517

Orthotopic liver transplantation: an experimental study on the prevention of infections with Gram-negative organisms

S. W. SCHALM, D. T. POPESCU, D. VAN DER WAAY, R. A. F. KROM, W. D. H. HENDRIKS, J. L. TERPSTRA AND C. JERUSALEM*

SUMMARY

Infection with Gram-negative bacteria is frequently the cause of death in human liver transplantation. In experimental liver transplantation in mongrel dogs we detected Gram-negative septicaemia in 73 per cent of our first 15 cases; maximal survival was 26 days.

In a second series of 27 orthotopic liver transplantations in tissue-typed littermate dogs and littermate pigs the standard surgical technique and aftercare were changed with regard to four factors: an end-to-end common bile duct anastomosis was made instead of a gallbladder to duodenum anastomosis; the continuous postoperative bacteriostatic antibiotic therapy was changed to a single 2-day course of bactericidal antibiotics; preoperative selective bowel decontamination combined with postoperative protective isolation was introduced; the dosage of azathioprine used for immunosuppression was reduced.

Infectious complications decreased markedly to 8 per cent, with survival beyond 1 year in 37 per cent of the animals. Therefore under experimental conditions Gram-negative septicaemia can be prevented in liver transplantation; whether all the factors cited above are important in this regard remains to be determined.

INFECTION with Gram-negative organisms is common after liver transplantation and frequently is a major cause of death (Fulginiti et al., 1968; Starzl, 1969; Murray-Lyon et al., 1970; Williams et al., 1973). In our laboratory death due to sepsis with Gram-negative micro-organisms (liver abscesses and cholangitis) occurred in 73 per cent of mongrel dogs with a liver transplant in spite of continuous systemic antibiotic treatment as advocated by Brettschneider et al. (1968). This incidence of lethal infectious complications contrasts with the results of Brettschneider et al., who reported long term survival in 6 out of 12 dogs when intensive immunosuppression was combined with continuous antibiotic treatment.

This report concerns an experimental study designed to reduce infections with Gram-negative bacteria in animals with a liver transplant. Our standard surgical technique and aftercare, which closely resembled that of Brettschneider et al. (1968), was changed as follows: a common bile duct to common bile duct anastomosis was performed instead of a gallbladder to duodenum anastomosis; intensive preoperative selective bowel decontamination and postoperative protective isolation for 1 month were introduced; bactericidal antibiotics (ampicillin/gentamycin) only on the day of surgery and the next day replaced the continuous antibiotic regimen with the bacteriostatic chloramphenicol; the azathioprine dose was lowered from 4 mg to 1–2 mg/kg day^{-1}, as tissue-typed littermate dogs and littermate pigs were used as experimental animals.

The marked decrease in infectious complications obtained in this series of experiments appears to justify publication of our findings. It should stimulate controlled investigations on how human liver transplant recipients should be managed to prevent lethal Gram-negative sepsis.

Materials and methods

Experimental groups (Table I)

Group I comprises 15 mongrel dogs with survival beyond 5 days in which surgical technique and aftercare were almost identical to those of Brettschneider et al. (1968) with the exception that (*a*) neomycin was administered preoperatively (2 × 1 g on day − 1) and postoperatively (2 × 250 mg for 14 days), and (*b*) antilymphocyte globulin treatment was not given. Biliary drainage was accomplished by gallbladder to duodenum anastomosis. Azathioprine (Imuran) was administered postoperatively in a dosage of about 4 mg/kg day^{-1} orally. Chloramphenicol 250 mg twice daily was given intravenously during surgery and thereafter orally.

Groups II and III encompass 15 littermate dog pairs with identical lymphocyte typing (Vriesendorp et al., 1971) and 12 littermate pig pairs respectively. The details of anaesthesia, metabolic care (Popescu, 1973) and the surgical technique are described elsewhere (Krom, 1975). Relevant details concerning animal care, the type of biliary drainage and antibiotic and immunosuppressive treatment are given below.

The dogs in group II received 3 × 5 g neomycin and 3 × 5 g streptomycin orally on the day before the operation. Biliary drainage was by end-to-end common duct anastomosis over an internal splint (*Fig.* 1). Postoperative azathioprine treatment was

---

* Departments of Internal Medicine, Surgery and Anaesthesiology, University Hospital, Leiden, Holland, the Radiobiological Institute TNO, Rijswijk, Holland, and the Departments of Cytology and Histology, University of Nijmegen, Holland.

Present address of S. W. Schalm: Gastroenterology Unit, Mayo Clinic, Rochester, Minn. 55901, USA.

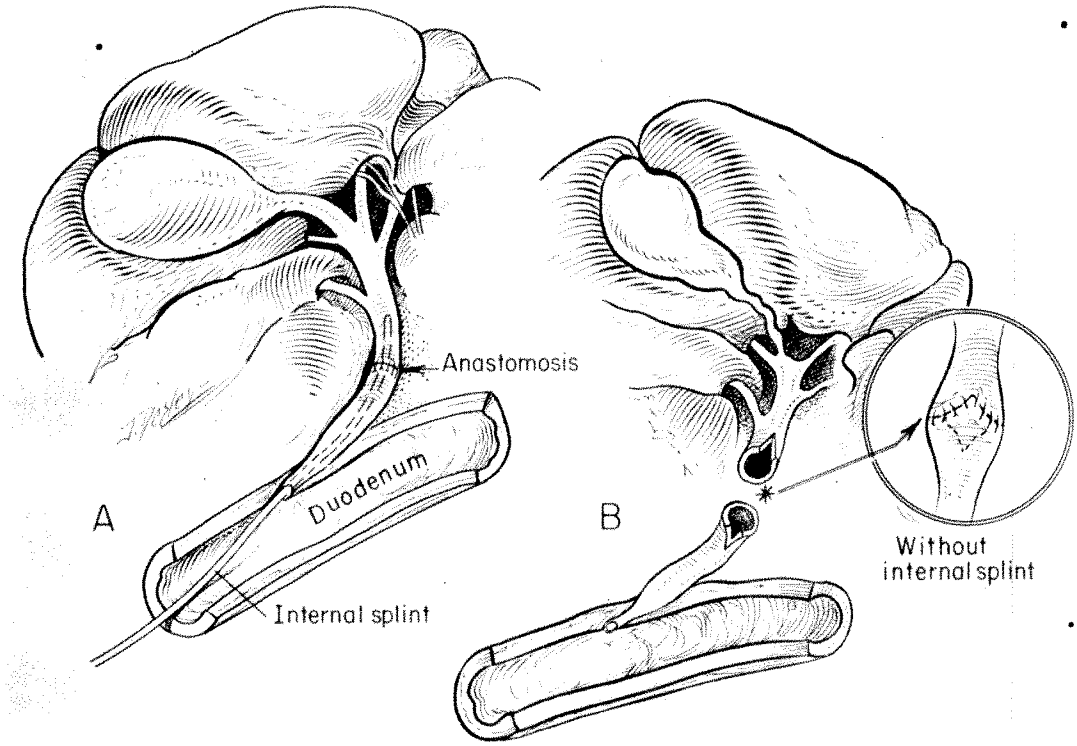


Fig. 1. Diagram of end-to-end common duct anastomosis. *A*, Anastomosis over an internal splint. *B*, Anastomosis with lumen-widening plasty (spatulation) without splinting or drainage.

Table I: SUMMARY OF THE TREATMENT OF THE THREE GROUPS

Group	No. of experiments	Species	Bile duct anastomosis	Antibiotics: Non-resorbable	Antibiotics: Systemic	Azathioprine dose	Protective isolation
I	15	Dogs, mongrel	GB-D	Neomycin 3 g	Chloramphenicol	4–5 mg/kg	No
II	15	Dogs, littermates, tissue-typed	CBD-CBD, internal splint	Neomycin 15 g, streptomycin 15 g	Ampicillin, gentamicin	2–2·5 mg/kg	Yes
III	12	Pigs, littermates	CBD-CBD, spatulation, no splint	Neomycin 15 g, kanamycin 15 g	Ampicillin, gentamicin	1 mg/kg	Yes

GB-D, Gallbladder to duodenum anastomosis.
CBD-CBD, End-to-end common bile duct anastomosis.

2 mg/kg day^{-1} per os. Ampicillin (2 × 30–50 mg) and gentamicin (2 × 2–3 mg/kg day^{-1}) were given intramuscularly only on day 0 and day 1. On the day before the operation the animal was placed in a room where protective isolation was maintained. Fresh air from outside was blown into the room, creating a pressure gradient over the entry to the room. Operating theatre shoes, gowns and gloves were worn by those entering the room. Tosylchloramine 2 per cent was used for disinfection and cleaning. Postoperatively, the animal received fresh tap water twice daily and sterile food pellets (Hope Farms) which had been autoclaved at 1 atmosphere for 10 minutes. Protective isolation was maintained for at least 1 month.

The pigs in group III received 3 × 5 g neomycin and 3 × 5 g kanamycin orally on the day before transplantation. Biliary drainage was by end-to-end common duct anastomosis with a lumen-widening technique (spatulation); no splint was used (*Fig.* 1). Systemic antibiotics and protective isolation were as in group II. In 4 animals postoperative protective isolation was limited to 1 week. The dose of azathioprine was 1 mg/kg day^{-1}. The data for all the groups are summarized in *Table I*.

Bacterial studies

All material for culture (except the faeces) was placed in trypticase soy broth bottles at 37 °C and observed for at least 7 days for aerobic and anaerobic growth. In group I bacterial studies were not performed systematically. In groups II and III the following investigations were done routinely in all the animals; however, satisfactory material for bacteriological investigations was not always obtained.

1. Samples of the liver and the donor's and recipient's common bile duct were taken for culture at surgery.
2. Blood cultures were taken on days 2 and 5 and thereafter when clinically indicated. Blood was obtained by puncture of a peripheral or jugular vein after washing and disinfecting the skin with 2 per cent iodine in 70 per cent alcohol.
3. Liver biopsies were attempted on day 5 and when clinically indicated. Half of the biopsy material was cultured. The liver biopsies were obtained by the percutaneous Menghini-needle technique after skin preparation as in 2.
4. Faeces were collected within 2 hours after excretion. The faecal sample was placed in a small plastic tube and frozen in liquid nitrogen. The antibiotic sensitivity of the faecal flora in a preoperative specimen was tested according to the method of van der Waay et al. (1970); in the postoperative specimens the total number of bacterial colonies belonging to the family Enterobacteriaceae was determined per gramme of faeces.
5. Complete autopsies were performed on all the animals in groups I, II and III. Macroscopic evidence of infection was defined as the finding of an abscess. Tissue samples of liver, gallbladder and sometimes other organs were taken for histological examination. On microscopic examination infection was assumed to be present when bacteria or abscesses were seen in tissue sections. For groups II and III an attempt was made to perform the autopsy within 2 hours after death; under aseptic conditions material for culture was obtained from the liver, and the heart was punctured for blood.

Results

Survival

In group I mean survival was 11 days with a range of 3–26 days, while in groups II and III mean survival amounted to 32 days* with 10 animals (37 per cent) surviving for 1 year. Except for one, all the animals surviving for 2 months lived longer than 1 year.

Incidence of bacterial infections (*Table II*)

Eleven of the 15 dogs of group I showed macroscopic or microscopic evidence of infection at autopsy. In the cases where positive cultures were obtained, either while alive or at autopsy. Gram-negative bacteria were found consistently. In the great majority of cases the infection was considered to be the major cause of death. In contrast, although cultures of the liver or common duct were positive at surgery in about 40 per cent of cases, definite evidence of postoperative infection was found in only 2 of the 27 animals of groups II and III; in only 1 animal was infection considered to be a major cause of death. The postoperative course of this animal was complicated by hematemesis on day 7; emergency vagotomy and pyloroplasty were carried out. The liver biopsy taken at the completion of surgery was positive for *Escherichia coli*. Three weeks later persistent bacteraemia (*E. coli*) developed. Response to chloramphenicol was excellent. Three months later the animal died during a rejection episode; a large subphrenic abscess was found in addition to histologically confirmed rejection. In the other animal with definite infection *Candida albicans* was found in the liver biopsy taken on day 14 and in the gallbladder at autopsy (culture and histology); the infection, however, was not considered of clinical importance.

No definite infections were diagnosed in any of the other 25 animals in groups II and III. However, *E. coli* was found in both liver and blood cultures in 4 animals at autopsy; 1 animal was found dead as a result of a necrotic small bowel volvulus 3 days after transplantation, while the other 3 animals died of hepatic failure (bilirubin > 10 mg per cent and the prothrombin time was prolonged more than three times) caused by rejection. Macroscopic or microscopic evidence of infection was not found at autopsy and blood cultures taken the day before death in 2 animals remained negative.

Response to attempted selective bowel decontamination differed in dogs and pigs (*Fig.* 2). All the dogs showed bloodstained diarrhoea on day 0. Enterobacteriaceae species were virtually absent in the faeces for about 2 days; after a week recolonization was almost completed. The response in pigs was much poorer. No diarrhoea was noticed in any of the animals; in only 3 of the 9 animals tested was a colony count of 10 Enterobacteriaceae species or less obtained. Retrospectively, sensitivity testing revealed that only 5 of the 9 animals were sensitive to the antibiotics given (neomycin/kanamycin); a combination of cephaloridine/neomycin showed excellent *in vitro* growth inhibition in nearly all the animals.

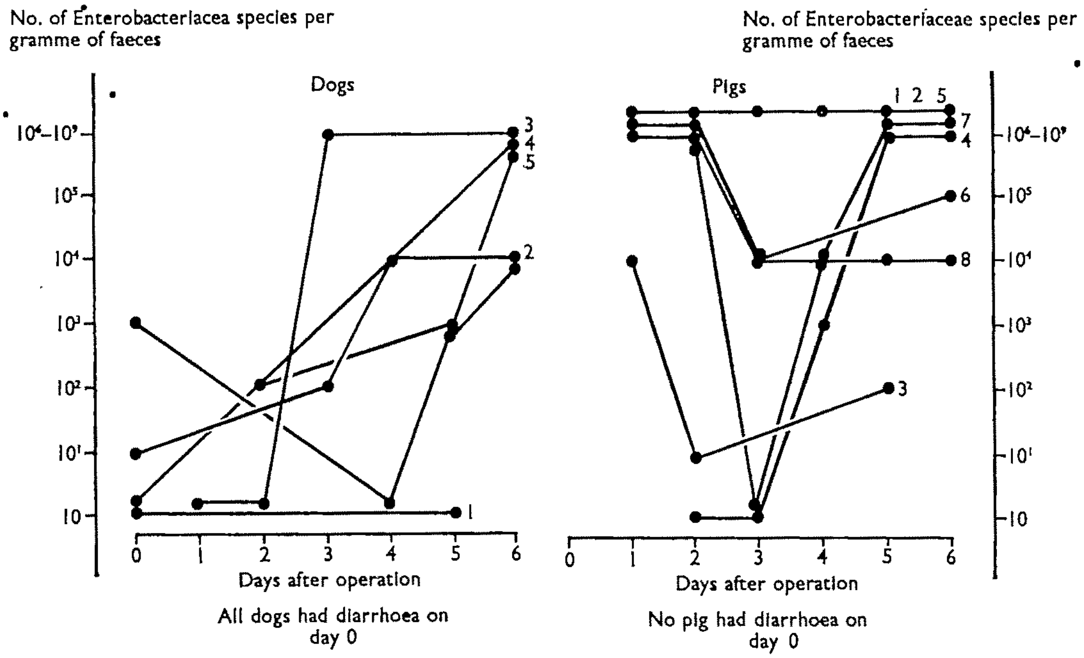
Discussion

Several important conclusions can be drawn from this prospective, albeit uncontrolled, study. In about 40 per cent of the cases Gram-negative bacteria were cultured from liver or bile duct samples taken during the operation. This emphasizes the necessity of antibiotic treatment in experimental liver transplantation. The adequacy of the 2-day systemic bactericidal antibiotic treatment is concluded from the fact that all the blood cultures were sterile on day 2. On day 5 only 1 of the 22 blood cultures was dubiously positive; all of the 15 liver cultures on that day were sterile.

A very low incidence of infections with Gram-negative bacteria was found in animals treated according to our new protocol, in comparison with experimental autotransplantation (Alican and Hardy, 1967) and homotransplantation experiments (MacSween, 1969; Dent et al., 1971). Clinically manifest cholangitis was never diagnosed with

---

* Maximal survival was arbitrarily determined as 60 days.



All dogs had diarrhoea on day 0

a

No pig had diarrhoea on day 0

b

Fig. 2. Effect of preoperative selective bowel decontamination and postoperative protective isolation on the number of colonies of Enterobacteriaceae species per gramme of faeces after liver transplantation in dogs (*a*) and pigs (*b*). Note the absence of response in pigs (nos. 1, 2, 5) with organisms resistant to the combination neomycin/kanamycin.

Table II: INCIDENCE OF POSITIVE CULTURES AT SURGERY, POSTOPERATIVELY OR AT AUTOPSY

Group	No. of animals	Liver/bile ducts culture at surgery	Blood cultures		Liver culture		Evidence of infection at at autopsy
			Day 5	Weeks 2–3	Day 5	Weeks 2–3	
I	15	2/8	0/3	2/3	1/1	1/1	11/15
II	15	6/15	1/11	0/6	0/12	1/3	1/9*
III	12	5/12	0/11	1/10	0/3	1/4	1/8†

* Six animals alive 1 year after transplantation.

† Four animals alive 1 year after transplantation.

certainty in groups II and III. Compared with a gallbladder to duodenum anastomosis, the end-to-end common bile duct anastomosis seemed to decrease the incidence of ascending cholangitis, as suggested by Calne (1969) and in accordance with the findings of Brettschneider et al. (1968) and Dent et al. (1971) in autotransplantation experiments in pigs. The feasibility of a common duct anastomosis without splinting or drainage has now been shown in pigs (Calne, 1969), monkeys (Myburgh et al., 1971) and dogs (Krom, 1975); in addition, in all our pigs in which the anastomosis was widened by the spatulation technique, absence of stenosis at the anastomosis site was documented by direct cholangiography. In our opinion this anastomosis should be reconsidered for human transplantations since ascending cholangitis may then be prevented. Liver abscesses were not found in the 27 experiments of groups II and III. One subphrenic abscess was probably a complication of the vagotomy and pyloroplasty operation performed because of a bleeding ulcer. Conceivably, selective decontamination of the bowel decreased portal bacteraemia during periods of liver ischaemia, i.e. the first few days after transplantation and when rejection occurs. Post-mortem liver and blood cultures were positive for *E. coli* in 4 animals, in contrast to the macroscopic and microscopic findings at autopsy. As in 2 animals a blood culture taken on the day before death did not show any growth, we assume that bacterial invasion was a preterminal event. It is of interest that in 3 animals it occurred together with severe hepatic failure due to rejection. In our opinion selective decontamination of the gut should not only be considered before transplantation but also when hepatic failure is diagnosed.

Selective decontamination of the bowel and protective isolation appeared to be rather simple procedures, when facilities for sensitivity testing of faecal flora are available. According to the colony counts in the postoperative faecal specimen, it was effective in nearly all the dogs. In most of the pigs the antibiotic combination neomycin/kanamycin chosen before the result of the sensitivity testing became available was not optimal; cephaloridin/neomycin was a superior combination *in vitro*. This finding emphasizes again the importance of adequate sensitivity testing of the faecal flora in order to obtain successful decontamination. Selective bowel decontamination can probably be performed in the relatively short period available before human liver transplantation; its effect might be enhanced by mechanical bowel preparation. No side effects other than diarrhoea were noted; no evidence was found that the procedure led to resistant strains or overgrowth with fungi or virus.

All the animals surviving for 2 months lived longer than 1 year and are still alive, except for the pig which died with a subphrenic abscess. The sustained survival contrasts with the experience of others; nearly all authors describe a steady decrease in the survival percentage with an increase in time. Although this decreasing survival percentage has been related to immunological processes, Alican and Hardy (1967) found a survival curve in autotransplantation experiments which appears to be identical to the allograft curves (Calne et al., 1969; Chandler et al., 1972). As infection was the main cause of death in the autotransplantation series, we also suspect infectious complications to be at least as lethal as rejection in the allotransplantation experiments. Consequently, the major factor responsible for the increase in long term survival in our experiments is the great reduction of Gram-negative infections in the acute and late phases of orthotopic liver transplantation.

The relative importance of the various measures used in this study to prevent infections with Gram-negative organisms is still open for discussion. The common duct to common duct anastomosis seems especially important to prevent chronic cholangitis, whereas bactericidal antibiotics and selective bowel decontamination with protective isolation prevent hepatic abscess formation and acute cholangitis with biliary fistula formation, both sequelae of septicaemia during transplantation or acute rejection episodes. Further studies are needed to assess the importance and necessity of these measures for the management of human liver transplant recipients.

Acknowledgements
The authors wish to thank D. L. Westbroek, H. M. Vriesendorp and J. van der Does for their help in obtaining littermate dogs identical according to lymphocyte typing. The investigation was supported by a grant from the Dutch Foundation for Medical Research.

References

ALICAN F. and HARDY J. D. (1967) Replantation of the liver in dogs. *J. Surg. Res.* **7**, 368–375.

BRETTSCHNEIDER L., TONG J. L., BOOSE D. S., DALOZE P. M., SMITH G. V., HUGUET C., BLANCHARD H., GROTH C. G. and STARZL T. E. (1968) Specific bacteriologic problems after orthotopic liver transplantation in dogs and pigs. *Arch. Surg.* **97**, 313–322.

CALNE R. Y. (1969) Surgical aspects of clinical liver transplantation in 14 cases. *Br. J. Surg.* **56**, 729–736.

CALNE R. Y., WHITE H. J. O., BINNS R. M., HERBERTSON B. M., MILLARD P. R., PENA J., SALAMAN J. R., SAMUEL J. R. and DAVIS D. R. (1969) Immunosuppressive effects of the orthotopically transplanted porcine liver. *Transplant. Proc.* **1**, 321–324.

CHANDLER J. G., VILLAR H., LEE S., WILLIAMS R. J., NAKAGI N. T., FERREBEE J. W. and ORLOFF M. J. (1972) The influence of histocompatibility matching according to lymphocyte types on orthotopic liver transplantation in dogs. *Surgery* **71**, 807–816.

DENT D. M., HICKMAN R., UYS C. J., SAUNDERS S. and TERBLANCHE J. (1971) The natural history of liver allo- and autotransplantation in the pig. *Br. J. Surg.* **58**, 407–413.

FULGINITI V. A., SCHRIBNER R., GROTH C. G., PUTNAM C. W., BRETTSCHNEIDER L., GILBERT S., PORTER K. A. and STARZL T. E. (1968) Infections in recipients of liver homografts. *New Engl. J. Med.* **279**, 619–626.

KROM R. A. F. (1975) Unpublished observations.

MACSWEEN R. N. M. (1969) Hepatic sepsis after liver transplantation in dogs and pigs. *Arch. Pathol.* **88**, 166–170.

MURRAY-LYON I. M., EVANS D. B., FOSTER W. D., HOLDEN R. U., RAKE M. O., STERN H., CALNE R. Y. and WILLIAMS R. (1970) Liver transplantation in man. The significance, patterns and control of infection. *Br. J. Surg.* **57**, 280–284.

MYBURGH J. A., ABRAHAMS C., MENDELSOHN D., MIENY C. J. and BERSOHN I. (1971) Cholestatic phenomenon in hepatic allograft rejection in the primate. *Transplant. Proc.* **3**, 501–504.

POPESCU D. T. (1973) Anaesthetic and homeostatic problems in experimental orthotopic liver transplantation in dogs. PhD Thesis, University of Leiden, Holland.

STARZL T. E. (1969) *Experience in Hepatic Transplantation.* Philadelphia, Saunders, pp. 329–347.

VAN DER WAAY D., DE VRIES J. M. and LEKKERKERK J. E. C. (1970) Eliminating bacteria from monkeys with antibiotics. In: BALNER H. and BEVERIDGE E. (ed.) *Infections and Immunosuppression in Subhuman Primates.* Munskgaard, Copenhagen, pp. 21–33.

VRIESENDORP H. M., ROTHENGATHER C., BOS E., WESTBROOK D. L. and VAN ROOD J. J. (1971) The production and evaluation of dog allo-lymphocytotoxins for donor selection in transplantation experiments. *Transplantation* **11**, 440–455.

WILLIAMS R., SMITH M., SHILKIN K. B., HERBERTSON B., JOYSEY V. and CALNE R. Y. (1973) Liver transplantation in man: the frequency of rejection, biliary tract complications, and recurrence of malignancy based on analysis of 26 cases. *Gastroenterology* **64**, 1026–1048.

Br. J. Surg. Vol. 62 (1975) 518–519

Fatal *Clostridium welchii* septicaemia following acute cholecystitis

M. T. CLANCY AND S. O'BRIAIN*

SUMMARY

A case of Clostridium welchii septicaemia following acute cholecystitis is described. The onset was acute and a rapidly fatal outcome ensued. Radiological findings were negative. An approach to the antibiotic treatment and general management is discussed.

THE commonest bacteria isolated from the biliary tract are the aerobic enteric bacteria and facultative streptococci. Among the anaerobes isolated, anaerobic streptococci and *Clostridium* species are the most prominent (Gorback and Bartlett, 1974). In the pre-antibiotic era some investigators found *Cl. welchii* in 10–20 per cent of diseased gallbladders at surgery (Gordon-Taylor and Whitby, 1930). Acute cholecystitis accompanied by *Cl. welchii* septicaemia is rare. The present case is reported to emphasize the serious nature of *Cl. welchii* cholecystitis, the difficulty in establishing a clinical diagnosis and the need to include an appropriate antibiotic in the treatment of this condition.

Case report

A 65-year-old male was admitted to hospital on 2 September 1973 with a 3-day history of right-sided abdominal pain radiating through to the back and shoulders and accompanied by vomiting. He had suffered two similar episodes in the preceding 3 months.

On examination the patient was anicteric, drowsy and flushed. The temperature was 37·3 °C, pulse rate 110/min, blood pressure 170/105 and respiratory rate 24/min. On abdominal examination there was marked tenderness and guarding in the epigastrium and right hypochondrium. Bilateral crepitations were heard at both lung bases. A diagnosis of acute cholecystitis was made.

Investigations carried out were: haemoglobin 16·2 g/dl, WCC $8000/\text{cm}^3$, ESR 25 mm/h; urea and electrolytes were normal except for a serum chloride of 97 mmol/l. Straight X-rays of the abdomen, both erect and supine, showed no evidence of perforation or intestinal obstruction and the gallbladder was not visualized. The chest X-ray showed areas of pneumonia at both bases. Further biochemical investigations were performed on the following day: total serum bilirubin 8·9 mg/100 ml, serum alkaline phosphatase 115 mu./ml, LDH 350 mu./ml, SGOT 154 mu./ml, urea 74 mg/100 ml, potassium 7·8 mmol/l. Serum estimations of chloride, SGOT, amylase and proteins were normal.

On admission the patient was judged to be sufficiently well to be treated with oral tetracycline and probanthine. Eight hours following admission he became dehydrated, drowsy and flushed. His temperature rose to 38·4 °C, pulse rate 130/min, blood pressure 200/110 and the respiratory rate 24/min. A blood culture was taken and he was treated with intravenous fluids and tetracycline. The following morning he had developed jaundice and was clinically shocked. A bluish discoloration of the abdominal wall had developed. Cephaloridine intravenously was started, but his condition deteriorated rapidly and he died less than 24 hours after admission. The following day the laboratory reported that the blood culture grew *Cl. welchii*, Type A, producing alpha and kappa toxins and sensitive to penicillin 2 units, ampicillin 10 µg, cephaloridine 5 µg, erythromycin 15 µg, co-trimoxazole 25 µg and rifamide 10 µg, and resistant to kanamycin 30 µg and tetracycline 10 µg.

At post-mortem examination there was evidence of acute cholecystitis, ascending cholangitis and septicaemia. The gallbladder was thickened and inflamed, containing soft mixed stones, bile and cloudy pale fluid. *Cl. welchii*, Type A, having the same antibiotic sensitivity pattern as the ante-mortem blood culture, was isolated from the gallbladder contents. The common bile duct was slightly dilated and contained soft mixed stones. Several small abscesses were present in the liver. Sections of the gallbladder wall showed extensive oedema and infiltration with polymorphs and mononuclear cells. Sections of the spleen showed a decrease in the numbers of polymorphs in the red pulp, and clostridia were seen lying in the splenic vessels (*Fig.* 1). The only other significant finding was pulmonary oedema.

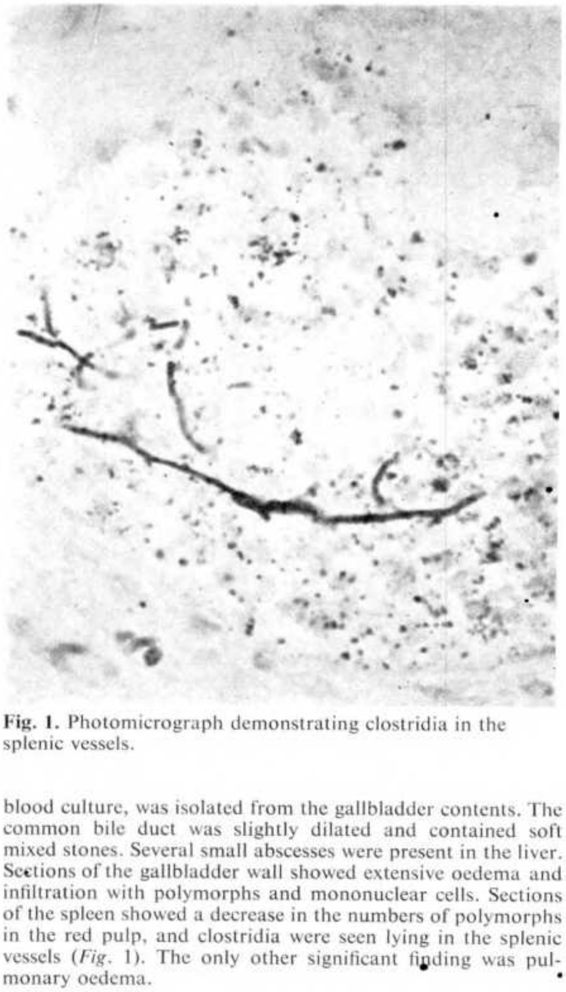


Fig. 1. Photomicrograph demonstrating clostridia in the splenic vessels.

Discussion

Reports of acute cholecystitis with *Cl. welchii* septicaemia are rare and those recorded are set out in *Table I*. The high mortality is noteworthy. Some

---

* Departments of Medical Microbiology and Histopathology, Federated Dublin Voluntary Hospitals and Trinity College, Dublin.

Table I: REPORTED CASES OF *CL. WELCHII* SEPTICAEMIA FOLLOWING ACUTE CHOLECYSTITIS

Author	No. of cases	
	Died	Survived
Elliot-Smith and Ellis (1957)	0	1
Pyrtek and Bartus (1962)	3	1
Turner (1964)	1	0
Bennett and Healey (1965)	0	1

unusual features have been described by various authors. In the largest group described by Pyrtek and Bartus (1962), they observed a gradual fall in blood pressure, accompanied by a rising temperature and a disproportionate increase in pulse rate. Bennett and Healey (1963) described acute spherocytic haemolytic anaemia occurring with *Cl. welchii* septicaemia. McKibbin and Parks (1974) reviewed the features of acute emphysematous cholecystitis. This is the terminology most frequently used. A wide variety of organisms has been discovered in reported cases, but at least 50 per cent of cultures revealed a growth of one of the clostridia (Bigler, 1960). McKibbin and Parks (1974) emphasized the importance of demonstrating gas in the gallbladder on a straight X-ray of of the abdomen which is usually evident within 24–48 hours of the onset of symptoms.

All of these reported features were absent in the present case, which raises the importance of early effective antibiotic therapy to include an anticlostridial agent when treating infections of the biliary tract. Unfortunately, X-rays of the abdomen were not repeated in this patient when he suddenly deteriorated 8 hours after admission. Almost certainly a diagnosis of acute cholecystitis due to gas-forming organism would have been made. The bluish discoloration of the abdominal wall which appeared was thought to be indicative of acute pancreatitis. In the light of the post-mortem findings this was, of course, a rapidly spreading myositis of the anterior abdominal wall, and the presence of crepitus over these areas was not recorded.

If these signs had been elicited, and the diagnosis of clostridial septicaemia suspected, prompt intervention with high doses of crystalline penicillin and ampicillin intravenously, to which *Cl. welchii* is extremely sensitive, could have been life saving. The choice of a tetracycline in the early management of this patient was unfortunate; although excreted mainly in the bile many strains are resistant (Johnstone and Cockcroft, 1968), and its use is contraindicated in the presence of jaundice and clinical shock. The changeover to an intravenous cephalosporin came too late; although the minimal inhibitory concentration of *Cl. welchii* for a cephalosporin is 0·4 µg/ml and for penicillin 0·12 µg/ml, the latter still remains the antibiotic of choice in the therapy of anaerobic infections due to this gas-forming organism. Finally, it is regrettable that facilities for the use of hyperbaric oxygen were not available. It is particularly effective in reducing the mortality from gas gangrene by preventing the production of alpha toxin and bacterial reproduction.

Acknowledgements

We wish to thank Mr J. Matthews for permission to publish this case and Dr C. T. Keane, Consultant Microbiologist, Federated Dublin Voluntary Hospitals, for his helpful advice.

References

BENNETT J. M. and HEALEY P. J. M. (1963) Spherocytic hemolytic anemia and acute cholecystitis caused by *Clostridium welchii. New Engl. J. Med.* **268**, 1070–1072.

BIGLER F. C. (1960) Acute gaseous cholecystitis. *Am. J. Med.* **29**, 181–186.

ELLIOT-SMITH A. and ELLIS H. (1957) *Clostridium welchii* infection following cholecystectomy. *Lancet* **2**, 723.

GORBACK S. L. and BARTLETT J. G. (1974) Anerobic infections. Part 1. *New Engl. J. Med.* **290**, 1177–1184.

GORDON-TAYLOR G. and WHITBY L. E. H. (1930) A bacteriological study of fifty cases of cholecystectomy with special reference to anaerobic infections. *Br. J. Surg.* **18**, 78–83.

JOHNSTONE F. R. C. and COCKROFT W. H. (1968) *Clostridium welchii* resistance to tetracycline. *Lancet* **1**, 660–661.

MCKIBBIN A. and PARKS T. G. (1974) Acute emphysematous cholecystitis. *Postgrad. Med. J.* **50**, 50–53.

PYRTEK L. J. and BARTUS S. H. (1962) *Clostridium welchii* injection complicating biliary-tract surgery. *New Engl. J. Med.* **266**, 689–693.

TURNER P. F. (1964) Fatal *Clostridium welchii* septicaemia following cholecystectomy. *Am. J. Surg.* **108**, 3–7.

Br. J. Surg. Vol. 62 (1975) 520–523

The removal of retained gallstones from the common bile duct: experience with sodium cholate infusion and the Burhenne catheter

D. C. BRITTON, B. S. GILL, R. M. R. TAYLOR AND OLIVER JAMES*

SUMMARY

The use of cholic acid T tube infusion and of the Burhenne catheter has been investigated in the management of gallstones retained in the common bile duct following biliary surgery in 9 patients. Four of 7 patients treated with cholic acid infusion showed disappearance of the stones during treatment. The stones in a fifth subject were removed by a combination of cholic acid infusion (1 stone disappeared) and instrumentation with a Burhenne catheter (a second stone removed). Use of a Burhenne catheter was unsuccessful in 3 of 4 patients. Details of the technique of cholic acid infusion are given, and possible complications of the treatment are discussed. The use of cholic acid infusion for the dissolution of stones in the common bile duct is recommended.

In spite of the use of routine preoperative cholangiography (Lawson and Gunn, 1970; McEvedy, 1970; Wheeler et al., 1970), Fogarty biliary balloon probes (Fogarty et al., 1968) and fibre-optic choledochoscopy, calculi retained in the biliary tree after gallbladder surgery are still a serious problem. Stones are left in the common bile duct in over 2 per cent of biliary tract operations (Colcock and McManus, 1955; Magee and Macduffee, 1968; Sandblom, 1972; Way et al., 1972). In some instances retained stones are discovered by postoperative cholangiography. In others the presence of an impacted stone may be known to the surgeon before completion of an operation but further trauma to the common bile duct is deemed inadvisable. In a few cases falsely interpreted peroperative cholangiography has led to error.

Retained stones may pass spontaneously following an operation while the T tube is still in position, but if they do not, surgical removal has, in the past, been necessary. This may be a difficult undertaking and has led to the use of such supplementary primary procedures as biliary fenestration (Capper, 1961; Margarey, 1966) or routine transduodenal sphincterotomy to avoid the need for re-exploration.

Recently, two techniques have been reported which may allow removal of retained calculi via the T tube or T tube tract without further surgery. The first is the instrumental removal of the stone via the T tube tract (Mazzariello, 1970; Margarey, 1971; Burhenne, 1973); the second depends upon the dissolution of the stones by instillation of bile salts down the T tube (Way et al., 1972; Lansford et al., 1974).

In this paper the use of sodium cholate infusion, manipulation of stones with a Burhenne catheter and a combination of these methods is reported in the management of 9 patients with stones retained in the common bile duct referred by a number of surgeons.

Patients and methods

Nine patients were studied 3–16 weeks after cholecystectomy and exploration of the common bile duct. In 6 subjects the stones were distal to the T tube. In all the patients the stones were radiolucent and had been demonstrated in at least two T tube cholangiograms prior to treatment. Liver function tests (serum alkaline phosphatase, SGOT and bilirubin) showed consistent obstructive features before treatment in each case. Informed consent to the procedures was obtained from each patient.

Sodium cholate infusion (Way et al., 1972)

Four patients received infusions of sodium cholate alone, 3 patients received infusion of sodium cholate followed by instrumentation with a Burhenne catheter and 2 patients had instrumentation with a Burhenne catheter alone.

A sterile solution of 100 mM sodium cholate buffered to pH 7·5 was prepared as follows: cholic acid 408 g, sodium hydroxide 38 g, sodium chloride 90 g and distilled water to 10 litres.

The irrigation fluid is manufactured using cholic acid (Biochemical grade; Weddell Pharmaceutical). If the pH of the final solution is found to be slightly acid, it is adjusted using sodium hydroxide to pH 7·5. On occasion the pH has been found to be on the alkaline side of 7·5. In this case it is adjusted to pH 7·5 using up to 14 g of extra cholic acid. This gives a 3·5 per cent excess of cholic acid. The irrigation fluid is then sterilized by filtration through a Sartorius Membranfilter 'Speed flow system', SM162/68. The pressure filter holder containing a Membranfilter pore size 0·45 μ and 142 mm diameter is sterilized by autoclaving at 121 °C and 151 p.s.i. for 30 minutes.

A long radio-opaque intravenous catheter (E–Z Cath 2254 16 Ga 18 in Deseret) was passed down the T tube under fluoroscopic control to the junction of the T tube, and the catheter was tightly secured in position to avoid leakage of sodium cholate back out of the T tube. The catheter was connected to the sodium cholate solution via central venous pressure manometer tubing. The vertical manometer tube was

---

* Department of Surgery and Gastroenterology Group, Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne.

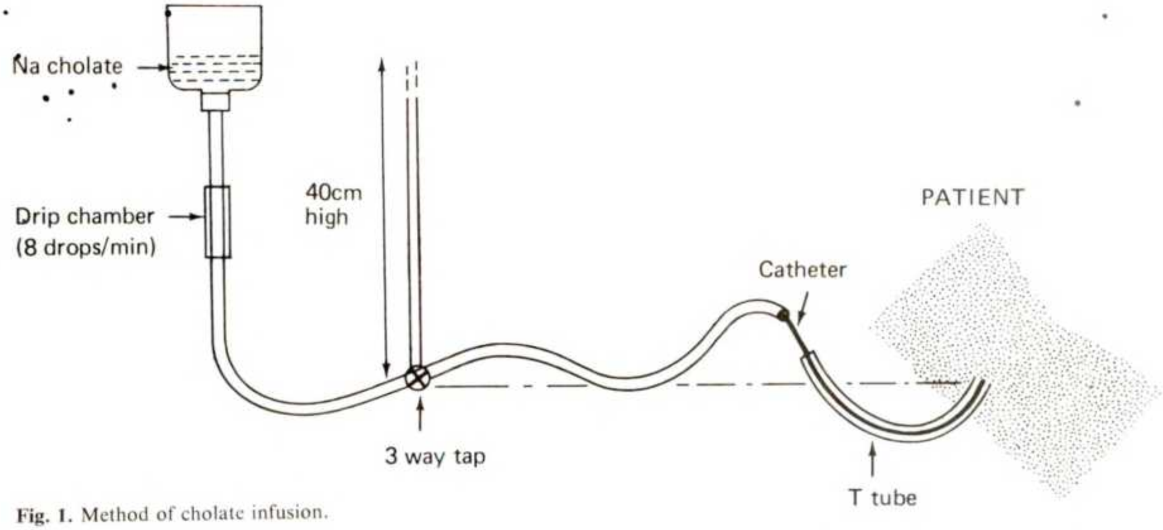


Fig. 1. Method of cholate infusion.

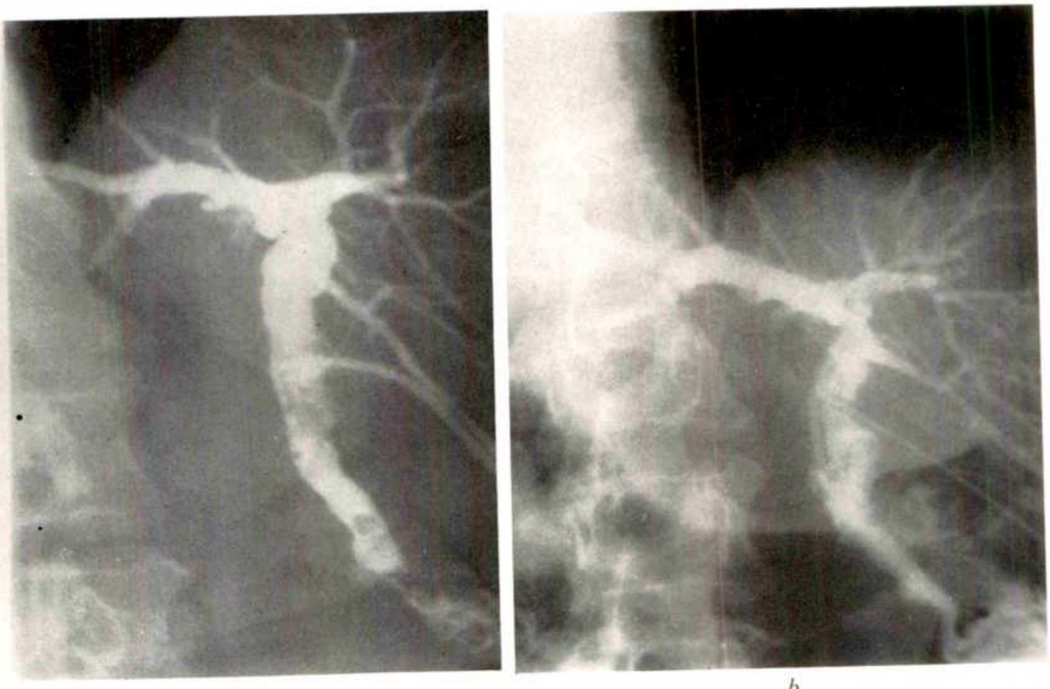


Fig. 2. T tube cholangiograms before (*a*) and after (*b*) sodium cholate infusion. Note three opacities at the lower end of the common bile duct in *a*.

kept in continuity with the system and was shortened to provide free overflow at about 40 cm above the common bile duct (*Fig.* 1). A flow rate of approximately 30 ml/h (8 drops/min) was used. The infusion was continued for up to 12 days. Cholangiograms were carried out at intervals of 4 days.

Daily estimations of liver function tests, serum electrolytes and serum amylase were carried out. Cholestyramine 4 g 3-hourly was given from the start of treatment. Metoclopramide 10 mg was given if vomiting occurred. If a patient reported pain the infusion was stopped until the pain settled. If the manometric pressure exceeded 40 mm of the solution and overflow from the top of the manometer occurred the infusion was stopped and the catheter was aspirated. Plugs of mucus were removed frequently from the common bile duct.

*Burhenne catheter**

The T tube was removed after confirmatory T tube cholangiography. The Burhenne catheter was then passed down the T tube tract under image intensification control and manipulated into the common bile

---

* Burhenne System, BSR 1 A Medi Tech, Cooper Scientific Corporation, Watertown, Mass., USA.

Table I: RESULTS OF TREATMENT

Treatment	Case	Site of stone(s)	Result
Sodium cholate infusion	1	Distal	Successful
	2	Distal	Successful
	3	Distal	Successful
	4	Distal	Successful
Sodium cholate infusion + Burhenne catheter	5	Proximal + distal	Sodium cholate 'removed' distal stone; Burhenne catheter removed proximal stone—successful
	6	Mobile	Sodium cholate failed; Burhenne catheter successful
	7	Proximal	Failed
Burhenne catheter	8	Proximal	Failed
		Distal	Failed

Table II: COMPLICATIONS AND SIDE EFFECTS

Treatment	Complication	No. of patients affected
Sodium cholate infusion	Diarrhoea	7/7
	Vomiting	7/7
	Pain + ? ampullary impaction	4/7
Burhenne catheter	Biliary peritonitis	1/5

duct. A Dormia basket was passed through the catheter, the stones were ensnared in the mesh of the basket and the basket was removed. If the procedure was successful liver function tests and repeat cholangiography were carried out. In unsuccessful cases laparotomy and re-exploration of the common bile duct were undertaken.

Results

In 4 out of 7 patients initially treated with sodium cholate solution the stones disappeared 8–12 days after starting the infusion (*Fig.* 2, *Table I*). In a further subject one stone disappeared following infusion but a second larger stone just proximal to the T tube failed to disappear; this stone was successfully removed by a Burhenne catheter. In a sixth patient sodium cholate infusion was ineffective but instrumentation succeeded in removing the stone. Two attempts at using a Burhenne catheter alone failed. In one of these subjects the stone was firmly impacted at the ampulla of Vater.

Complications and side effects

All the patients treated with sodium cholate experienced diarrhoea (*Table II*); this was lessened by the use of cholestyramine but was often quite severe. All the patients who received sodium cholate also became nauseated, anorexic and vomited intermittently despite treatment with metoclopramide. Although 4 of the 7 patients experienced abdominal pain at some time during the infusion this was never severe and in no case was there an associated elevation of serum amylase. In 1 subject successful treatment of the common bile duct stones with sodium cholate solution was followed by biliary peritonitis after removal of the plastic T tube. At operation moderate fibrosis around the common bile duct was found. A further case o biliary peritonitis occurred 2 hours after use of Burhenne catheter and Dormia basket. This wa thought to be due to rupture of the T tube tract. Ther were no deaths or long term complications.

Discussion

It is now widely recognized that peroperative cholangiography should be carried out during all routin cholecystectomies. In patients in whom the commo bile duct has been explored and T tubes inserted int the duct it is important to perform cholangiograph via the T tube before the operation is conclude rather than 1 week later. Radiology used in this wa may reduce the frequency with which gallstones ar mistakenly left in the common bile duct. Nevertheless cases will still occur and any method of removin retained gallstones without a second laparotomy i worth investigating.

While several substances have, in the past, been said to dissolve cholesterol gallstones none has been proved to be effective. Earnest and Admirand (1971) and Farrell et al. (1973) have shown that cholesterol gallstones may be reduced by up to 35 per cent by weight when suspended in bile salt solutions. It is postulated that the effect of cholic acid infusion may be to reduce the size of stones and possibly to make them break into smaller particles which may then be passed out of the common bile duct. The action may, therefore, be a combination of dissolution and subsequent flushing out of the common bile duct. Farrell et al. (1973) showed that cholesterol stones dissolved more readily in bile salt and phospholipid mixtures than in bile salt solution alone. *In vivo* phospholipid is added to the system by the patient's own bile.

The main side effects of cholic acid infusion were nausea, vomiting and diarrhoea. All the patients felt unwell during the infusion, but no marked electrolyte disturbances were noted during treatment. Metoclopramide and cholestyramine alleviated symptoms of nausea and diarrhoea respectively.

Much attention has been focused on the possible hepatoxicity of the oral bile salts, but significant hepatotoxicity is extremely unlikely with cholic acid treatment since (*a*) it is only given for a short time, and (*b*) cholic acid is 7-α-dehydroxylated to deoxycholic acid in the colon; while chenodeoxycholic and particularly lithocholic acids have been shown to be hepatotoxic in many species (Palmer, 1972) the same has not been shown for cholic and deoxycholic acid. Liver function tests have remained normal for up to 1 year after treatment in all the patients following cholic acid infusion.

In neither instance where the stone was proximal to the T tube did dissolution with cholic acid occur (*Cases* 5 and 7). This confirms the finding of Lansford et al. (1974). It may be that this is because there is a poorer stream of cholic acid on these stones than on those distal to the T tube.

The use of the Burhenne catheter has been enthusiastically advocated by several authors with outstanding results. It was used in the present study on a very small number of patients but the results are not so encouraging. In 1 patient use of a Burhenne catheter led to a biliary peritonitis and subsequent laparotomy. However, in 2 subjects a Burhenne catheter was used to remove stones successfully following cholic acid treatment. If cholic acid treatment is considered this must be carried out before removal of the T tube and therefore before use of a Burhenne catheter and Dormia basket.

Conclusion

The objective of this paper was to provide a practical guide to surgeons who may infrequently encounter the problem of stones retained in the common bile duct following surgery. Use of sodium cholate infusion is simple and needs little expertise apart from the ability to manage side effects. The successful use of the Burhenne catheter, however, appears to require considerable practice and expertise and this instrument should perhaps be reserved for centres with particular interest in its use.

Acknowledgements

We wish to thank the Departments of Radiology (Dr C. K. Warrick) and Biochemistry (Professor A. L. Latner), Royal Victoria Infirmary, Newcastle upon Tyne, for very considerable help and cooperation in this study, and Miss J. Thompson for technical assistance.

We also thank Mr L. B. Fleming and Professor Ivan D. A. Johnston for much helpful advice and support.

References

BURHENNE H. J. (1973) Non-operative retained biliary tract stone extraction. *Am. J. Roentgenol.* **177**, 388–399.

CAPPER W. M. (1961) External choledochoduodenostomy. *Br. J. Surg.* **49**, 292–300.

COLCOCK B. P. and MCMANUS J. E. (1955) Experiences with 1356 cases of cholecystitis and cholelithiasis. *Surg. Gynecol. Obstet.* **101**, 161–172.

EARNEST D. L. and ADMIRAND W. H. (1971) The effects of individual bile salts in cholesterol solubilization and gallstone dissolution. *Gastroenterology* **60**, 772.

FARRELL K. E., SMITH D. C. and MACKAY C. (1973) Gallstone dissolution *in vitro*. *Br. J. Surg.* **60**, 900.

FOGARTY T. J., KRIPPACHINE W. M., DENNIS D. L. and FLETCHER W. S. (1968) Evaluation of an improved operative technique in common duct surgery. *Am. J. Surg.* **116**, 177–183.

LANSFORD C., MEHTA S. and KIEK F. jun. (1974) The treatment of retained stones in the common bile duct with sodium cholate infusion. *Gut* **15**, 48–51.

LAWSON R. A. M. and GUNN A. A. (1970) The value of operative cholangiography. *J. R. Coll. Surg. Edinb.* **15**, 222–227.

MCEVEDY B. V. (1970) Routine operative cholangiography. *Br. J. Surg.* **57**, 277–279.

MAGEE R. B. and MACDUFFEE R. C. (1968) One thousand consecutive cholecystectomies. *Arch. Surg.* **96**, 858–862.

MARGAREY C. J. (1971) Non surgical removal of retained biliary calculi. *Lancet* **1**, 1044–1046.

MARGAREY J. R. (1966) Biliary fenestration. *Br. J. Surg.* **53**, 41–46.

MAZZARIELLO R. (1970) Removal of residual biliary tract calculi without reoperation. *Surgery* **67**, 566–573.

PALMER R. H. (1972) Bile acids, liver injury and liver disease. *Arch. Intern. Med.* **130**, 606–617.

SANDBLOM P. (1972) In Discussion of paper by WAY et al. (1972).

WAY L. W., ADMIRAND W. H. and DUNPHY J. E. (1972) Management of choledocholithiasis. *Ann. Surg.* **176**, 347–359.

WHEELER M. H., RAKSASOCK S. and WILLIAMS J. A. (1970) Operative cholangiography, its effect on the practice of cholecystectomy. *Br. Med. J.* **4**, 161–164.

Br. J. Surg. Vol. 62 (1975) 524–527

Long term changes in total body water, total exchangeable sodium and total body potassium before and after ileostomy

G. L. HILL, J. C. GOLIGHER, A. H. SMITH AND W. S. J. MAIR*

SUMMARY

In 10 patients with inflammatory bowel disease, total body water, total body potassium and total exchangeable sodium were measured both before and 6 months after the establishment of a permanent ileostomy. All 10 patients underwent elective surgery for their inflammatory bowel disease but all were malnourished before surgery when their body composition was first measured.

Six months later, when the body composition was again determined, all the patients were in good health and had normally functioning ileostomies. As a group they had gained 6·8 kg in body weight and 372 mEq total body potassium over the 6-month period. When the 'normal' total body water was calculated for each patient, a deficit of 12·4 per cent for the group was found before surgery and this was still present (11·1 per cent) 6 months later. The concentration of exchangeable sodium in the body water fell from an abnormally high level before surgery to within the normal range 6 months later.

These data show that deficits in total body water occurring preoperatively are not repaired in the months following the establishment of a well-functioning ileostomy, and that a reduction of total exchangeable sodium is present in patients with an ileostomy who are otherwise well. It is suggested that these findings should encourage the surgeon managing patients with intractable inflammatory bowel disease to strive for good nutrition and normal body composition before embarking on excisional surgery and the establishment of a permanent ileostomy.

CONVALESCENCE after proctocolectomy and ileostomy for inflammatory bowel disease is usually marked by rapid weight gain and substantial improvement in the well-being of the patient. After some months he is usually back at work and living an almost normal life.

In spite of this apparent excellent health, there is strong evidence that ileostomy patients who are otherwise well are chronically dehydrated and sodium depleted. Not only has diminished renal excretion of water and sodium been demonstrated in ileostomy patients (Gallagher et al., 1962; Kanaghinis et al., 1963; Clarke et al., 1967) but direct studies of body composition have shown a reduction of total body water and a deficit in total exchangeable sodium (Clarke et al., 1967).

The present study, which measures body composition in a group of patients both before ileostomy and 6 months later, examines these changes in body composition more fully.

Patients and methods

Ten patients who underwent elective ileostomy for inflammatory bowel disease were investigated. Clinical data and the operation performed on each patient are shown in *Table I*. At the time of operation all the patients were chronically ill and unable to work because of the bowel symptoms. All had suffered considerable weight loss (*Table I*).

Total exchangeable sodium was measured by the method described by Veall and Vetter (*1958*) using the radioactive isotope ^{24}Na. Total body water was determined by the dilution of a volume of tritiated water estimated from two plasma samples taken 3 and 6 hours after oral administration. Total body potassium was measured by the whole body counter method described by Burkinshaw (1967) from these laboratories.

Two days prior to surgery each patient was interviewed, physically examined and weighed. Serum sodium and potassium were estimated using a Technicon Autoanalyzer (SMA/660). The total body potassium was then estimated using a whole body counter.

The following day, i.e. the day before surgery, 30 μCi ^{24}Na diluted in physiological saline and 200 μCi tritiated water were dispensed into a plastic cup and drunk together with several rinsings by the patient. At 3 and 6 hours later 10 ml of venous blood were taken and stored in a heparinized tube. The blood samples were distilled (Vaughan and Boling, 1961) and duplicate 1-ml aliquots were added to 10 ml NE220† and measured in a Packard Liquid Scintillation Counter (Series 300), together with appropriate standards and blanks. Total body water (TBW) was then calculated from the formula:

$$\text{TBW (litre)} = \frac{\text{Total counts of tritium administered}}{\text{Counts/litre of serum water (extrapolated to time of administration)}}.$$

Twenty-four hours after the administration of the sodium isotope, 20 ml of venous blood were taken and stored in a heparinized tube. The volume of the 24-hour urine collection was measured and a 10-ml aliquot taken for measurement. The ^{24}Na content of the serum and urine was measured using a NaI

---

* University Departments of Surgery and Nuclear Medicine, General Infirmary, Leeds.

† Nuclear Enterprises (GB) Ltd, Edinburgh.

Table I: CLINICAL DATA

Patient	Sex	Age	Estimated weight loss (kg)	Preoperative prednisone (mg/d)	Final diagnosis	Operation performed
1	F	58	36	45	Granulomatous disease	Ileostomy and proctocolectomy
2	F	63	8	10	Ulcerative colitis	Ileostomy and proctocolectomy
3	M	30	8	0	Ulcerative colitis	Ileostomy and proctocolectomy
4	F	41	6	0	Ulcerative colitis	Ileostomy and proctocolectomy
5	F	42	7	10	Ulcerative colitis	Ileostomy and proctocolectomy
6	M	26	20	40	Ulcerative colitis	Ileostomy, proctocolectomy and 18-cm ileal resection
7	M	27	17	10	Ulcerative colitis	Ileostomy, proctocolectomy and 68-cm ileal resection
8	M	33	13	0	Granulomatous disease	Ileostomy, right hemicolectomy and 120-cm ileal resection
9	M	31	10	0	Granulomatous disease	Ileostomy, right hemicolectomy and 60-cm ileal resection
10	M	38	13	0	Granulomatous disease	Ileostomy, proctocolectomy and 45-cm ileal resection

Table II: ABSOLUTE VALUES OF BODY COMPOSITION BEFORE AND 6 MONTHS AFTER ILEOSTOMY

	Before ileostomy				6 Months after ileostomy			
Patient	Body weight (kg)	TBW (l)	Na_E (mEq)	TBK (mEq)	Body weight (kg)	TBW (l)	Na_E (mEq)	TBK (mEq)
1	46·2	30·4	2701	2253	52·1	30·2	2766	2494
2	39·3	22·1	2033	1534	48·6	26·1	2187	1955
3	47·0	26·3	2223	2205	53·7	27·5	1768	2385
4	48·5	25·9	2073	2330	48·3	26·2	2135	2324
5	53·9	26·7	2348	2425	56·3	30·1	2751	2641
6	47·0	32·0	3282	2205	62·5	40·8	2471	3533
7	57·1	36·6	3130	3033	63·3	42·6	3240	3511
8	53·0	28·1	2583	2701	66·3	37·7	2802	3088
9	49·6	26·6	2170	2824	59·2	35·0	2740	3258
10	55·4	32·6	2337	2552	54·9	31·3	1964	2595
				Mean change	6·8	4·0	−5·6	372·2
				P	$<0·005$	$<0·02$	NS	$<0·02$
				% change	+13·7	+14·3	−0·2	+15·5

NS, Not significant.

scintillation counter together with appropriate standards and blanks. The concentration of sodium in the serum and urine was determined and the total exchangeable sodium (Na_E) was calculated from the formula:

$$Na_E = \text{Na space (litre)} \times \text{serum Na (mEq/litre)}.$$

For the total body water estimate the total experimental standard deviation, including dispensing calibration, counting and reproducibility, was not greater than ±3 per cent (Williams et al., 1964). The coefficient of variation of the estimate of total body potassium for a typical man was 3·2 per cent and for a typical woman 3·4 per cent (Burkinshaw, 1967).

Results

General health

At 6 months all the patients claimed good health and had either resumed or were about to resume their normal occupation. On physical examination each patient was found to be physically fit apart from an incompletely healed perineal wound in patient 6 and a degree of tiredness and depression in patient 10. There was no evidence of recurrent disease in any of the patients. A full blood count and serum electrolyte profile for each patient were within the normal ranges.

Body weight and total body potassium

Table II shows the changes in body weight over the 6-month period. Apart from patients 4 and 10 in whom the body weight remained at the preoperative level, the rest of the group had an appreciable weight gain. However, only 4 patients (2, 3, 8, 9) had returned to what they considered was their ideal pre-illness weight. The group as a whole had a mean weight gain of 13·7 per cent (6·8 kg, $P<0·005$) over the 6-month period. There was a similar increase in total body potassium. *Table II* shows that, apart from patients 4 and 10, the patients had a substantial gain in total body potassium when measured 6 months after the operation. The group of patients as a whole had an overall mean gain in total body potassium of 15·5 per cent (372 mEq, $P<0·02$) 6 months after surgery.

The total body potassium/total body water ratio (*Table III*) remained constant for each patient apart from patient 6, in whom the increase in ratio at 6 months indicates a return to a more normal value.

Total body water and 'normal' total body water

Table II shows that there has been a mean gain in total body water of 14·3 per cent (4 litres, $P<0·02$) for the group at 6 months. The ratio of total body water/body weight (*Table III*) remained constant for all the patients except patient 1, in whom a falling water fraction indicates a disproportionate gain in body fat and total body solids.

Table III: DERIVED BODY COMPOSITION RATIOS BEFORE AND 6 MONTHS AFTER ILEOSTOMY

	Before ileostomy			6 Months after ileostomy		
Patient	TBW/ body weight	$\mathrm{Na_E}$/ TBW	TBK/ TBW	TBW/ body weight	$\mathrm{Na_E}$/ TBW	TBK/ TBW
1	65·8	88·8	74·1	58·0	91·6	82·6
2	56·2	92·0	69·4	54·0	83·8	74·9
3	56·0	84·5	83·8	51·2	64·3	86·7
4	53·4	80·0	90·0	54·2	81·4	88·7
5	50·0	87·9	90·8	53·5	91·4	87·7
6	68·0	102·6	68·9	65·3	60·6	86·6
7	64·1	85·5	82·9	67·3	76·1	82·4
8	53·0	91·9	96·1	57·0	74·3	81·9
9	54·0	81·6	102·2	59·1	78·3	93·1
10	59·0	71·7	78·3	57·0	62·8	82·9
			Mean change	−0·3	−10·2	+0·7
			P	NS	0·05	NS
			% change	−0·5	−13·3	+0·8

NS, Not significant.

Table IV: COMPARISON OF 'NORMAL' TOTAL BODY WATER (NTBW)* AND THE MEASURED TOTAL BODY WATER (TBW)

	Before ileostomy		6 Months after ileostomy	
Patient	NTBW (l)	$\frac{\text{TBW}-\text{NTBW}}{\text{NTBW}}$	NTBW (l)	$\frac{\text{TBW}-\text{NTBW}}{\text{NTBW}}$
1	31·4	−0·032	33·8	−0·107
2	24·1	−0·083	28·3	−0·078
3	30·9	−0·149	32·7	−0·159
4	32·2	−0·196	32·1	−0·184
5	33·1	−0·193	35·3	−0·147
6	30·9	+0·036	44·4	−0·081
7	39·3	−0·069	44·2	−0·036
8	36·0	−0·219	39·9	−0·055
9	37·2	−0·285	41·6	−0·159
10	34·4	−0·052	34·9	−0·103
Mean		−0·124		−0·111
Mean change			+3·8	+0·043
P			<0·02	NS

* Derived from the equation:

$$\text{NTBW}^{(\text{L})} = (0{\cdot}0102 \pm 0{\cdot}027)\ \text{TBK} + 8{\cdot}40 \pm 3{\cdot}21.$$

Standard error estimate 5·6 per cent mean NTBW.
NS, Not significant.

The relationship between total body potassium and total body water is well known (Talso et al., 1960; Hughes et al., 1967; Delwaide and Crenier, 1973) and has been used to predict variations from normality, using the measured total body water to determine potassium deficiency (Hughes et al., 1967), and total body potassium to estimate water deficiency (Smith, 1965). Data obtained previously in this laboratory (Hughes et al., 1967) have been used to predict the 'normal' total body water of the 10 patients using their total body potassium measurement. The results shown in *Table IV* indicate a mean reduction in body water compared with the normal state of 12·4 per cent before ileostomy and 11·1 per cent 6 months after ileostomy.

Total exchangeable sodium

As a group the patients did not demonstrate an absolute increase in total exchangeable sodium over the 6-month period (*Table II*) although 3 individuals did so (patients 5, 8, 9).

The ratio of total exchangeable sodium/total body water (*Table III*) fell from an abnormally high level preoperatively (mean 86·7) to within the normal range (Moore et al., 1963) at 6 months (mean 76·5, $P<0{\cdot}05$).

The patients (1, 2, 5, 6, 7) (*Table I*) on steroids preoperatively had a higher total exchangeable sodium/total body water ratio when measured at this time than those not on steroids, although this difference is not statistically significant (91·4 ± 6, cf. 81·9 ± 7).

Discussion

Measurement of total exchangeable sodium, total body water and total body potassium revealed considerable variations from patient to patient. Nevertheless, it was possible to demonstrate that 6 months after ileostomy when nutritional equilibrium had been regained and the patients looked fit and well there were deficits in both total body water and total exchangeable sodium.

In spite of a mean weight gain of 6·8 kg and an increase in total body potassium of 372 mEq, a persisting deficit of 11–12 per cent of total body water remained 6 months after ileostomy. Whereas the concentration of sodium in body water was abnormally high preoperatively, this returned to within the normal range 6 months later. The normal total exchangeable sodium/total body water ratio at 6 months, together with a persisting reduction in total body water, indicates a deficit of total exchangeable sodium of similar magnitude to that of total body water. This deficit developed during the 6-month period following operation.

These findings of salt and water depletion occurring in patients with an ileostomy are in accord with a previous report (Clarke et al., 1967). This showed a 7 per cent deficit in total exchangeable sodium and an average reduction of 11 per cent in total body water in patients with a well-established ileostomy when compared with a control group.

The present study defines these deficits more completely. The total body water reduction is found in the preoperative colitic patient and persists after ileostomy, whereas the total exchangeable sodium deficit tends to develop after the ileostomy has been established.

Six months after ileostomy all the patients had normal ileostomy function and none appeared clinically dehydrated (Hill, Mair and Goligher 1974). Renal conservation of sodium was present in these patients, and those without an ileal resection showed intestinal conservation of sodium and water. Presumably, therefore, the failure to regain body water and the loss of body sodium are reflections of a chronic salt- and water-losing state to which the conservation processes of the body have responded incompletely. It is interesting that in colitic patients who have an ileorectal anastomosis instead of an ileostomy the rectum retains sufficient absorptive function that normal body composition is regained and maintained (Hill, Watts et al., 1974).

Thus it appears that a severe water deficit occurring in the colitic patient prior to surgery is not repaired after excision of the diseased bowel and a satisfactory ileostomy is established. This study supports the postulate that the water deficit is primary and the sodium changes alter in the months following surgery to regain normal body tonicity.

It is a clinical observation that the colitic patient who is nutritionally competent before surgery makes better progress and is stronger and healthier in the weeks and months following proctocolectomy than his counterpart who is severely malnourished at the time of operation. It seems probable that a water deficit is less likely to develop in the ileostomy patient who is nutritionally well prior to surgery, but we are unable to comment on this because none of the patients in the present study were hyperalimented before surgery, either by parenteral nutrition or by an elemental diet. Nevertheless, these data should encourage the surgeon managing patients with intractable inflammatory bowel disease to strive for good nutrition and normal body composition before embarking on excisional surgery and the establishment of a permanent ileostomy.

Acknowledgements

The authors express their appreciation to several colleagues for helpful discussion, to Dr L. Burkinshaw and Miss D. W. Krupowicz, Department of Medical Physics, for the whole body potassium measurements and to Dr C. J. Hayter, Consultant Physician, Department of Nuclear Medicine, for his continual encouragement.

References

BURKINSHAW L. (1967) Measurement of body potassium. Calibration and intercomparison of two whole-body radiation counters. *Phys. Med. Biol.* **12**, 477–488.

CLARKE A. M., CHIRNSIDE A., HILL G. L., POPE G. and STEWART M. K. (1967) Chronic dehydration and sodium depletion in patients with established ileostomies. *Lancet* **2**, 740–743.

DELWAIDE P. A. and CRENIER E. J. (1973) Body potassium as related to lean body mass measured by total water determination and by anthropometric method. *Hum. Biol.* **45**, 509.

GALLAGHER N. D., HARRISON D. D. and SKYRING A. P. (1962) Fluid and electrolyte disturbances in patients with long-established ileostomies. *Gut* **3**, 219–223.

HILL G. L., MAIR W. S. J. and GOLIGHER J. C. (1974) Impairment of ileostomy adaptation in patients after ileal resection. *Gut* **15**, 982–987.

HILL G. L., WATTS J. MCK., ISELI A., CLARKE A. M. and HUGHES E. S. R. (1974) Total body water and total exchangeable sodium in patients after ileorectal anastomosis. *Br. J. Surg.* **61**, 189–192.

HUGHES D., WILLIAMS R. E. and SMITH A. H. (1967) Clinical studies on whole-body potassium content measured by gamma-ray spectrometry in health and disease. *Clin. Sci.* **32**, 503–509.

KANAGHINIS T., LUBRAN M. and COGHILL N. F. (1963) The composition of ileostomy fluid. *Gut* **4**, 322–338.

MOORE F. D., OLESON K. H., MCMURREY J. D., PARKER H. V., BALL M. R. and BOYDEN C. M. (1963) *The Body Cell Mass and Its Supporting Environment.* Philadelphia, Saunders.

SMITH A. H. (1965) PhD Thesis, University of Leeds.

TALSO B. P. J., MILLER C. E., CARBELLO A. J. and VASQUEZ J. (1960) Exchangeable potassium as a parameter of body composition. *Metabolism* **9**, 456–471.

VAUGHAN B. E. and BOLING E. A. (1961) Rapid assay procedures for tritium-labeled water in body fluids. *J. Lab. Clin. Med.* **57**, 159–164.

VEALL N. and VETTER H. (1958) *Radioisotope Techniques in Clinical Research and Diagnosis.* London, Butterworths.

WILLIAMS R. E., SMITH A. H., YOUNG G. A., PARSONS F. M. and REED G. W. (1964) Experimental comparison of the rates and volumes of distribution of urea, creatinine N-acetyl-4-aminophenazone, and tritiated water. *Br. J. Surg.* **51**, 544–549.

Br. J. Surg. Vol. 62 (1975) 528–534

Results of surgery for Crohn's disease in the Glasgow region, 1961–70

S. YOUNG, I. S. SMITH, J. O'CONNOR, J. R. BELL AND G. GILLESPIE*

SUMMARY

During the period 1961–70, 283 patients in the Glasgow region have been studied with regard to the outcome of 418 surgical procedures performed for Crohn's disease.

Resection was followed by an overall recurrence rate of 33 per cent, but in disease confined to the large bowel the rate was 18 per cent.

Exploratory operations and bypass procedures were followed by a recurrence rate of 70 per cent. Evidence is provided that recurrence following bypass procedures for small bowel disease and ileocolitis occurs at a later stage than after exploratory operations alone.

By the end of the study period 77 per cent of patients in this series had required one or more resections.

CHRONIC Crohn's disease of the small or large bowel is a condition which tends to undergo spontaneous relapse and remission. Although supportive medical therapy may be helpful in providing symptomatic relief, it is not curative and most patients eventually come to operation (Colcock, 1964; Jones et al., 1966; Slaney, 1968; Banks et al., 1969; Edwards, 1969; de Dombal et al., 1974). As this disease has increased in incidence (Norlen et al., 1970; Fahrlander and Baerlocher, 1971; Kyle, 1971; Smith et al., 1975), the surgical management of the condition in the Glasgow region during the decade 1961–70 has been examined with particular reference to the mortality, morbidity and the likelihood of subsequent recurrence.

Patients and methods

For the purpose of this study the Glasgow region may be defined as that area in West Scotland 25 miles in diameter, centred on the City of Glasgow. The population of this area amounts to 1·7 millions, for whom hospital facilities are provided by 12 Health Service Hospitals. Patients admitted to these hospitals during the decade with a diagnosis of Crohn's disease were identified by reference to the inpatient hospital statistics of the Scottish Home and Health Department, which has recorded all Scottish hospital admissions since 1961.

Following examination of the case records, the diagnosis of Crohn's disease was accepted only if the clinical and radiological features were supported by histological features as described by Morson (1971) and/or operative appearances indicative of transmural inflammatory bowel disease. Thus, 283 patients who had undergone one or more surgical procedures varying from biopsy or laparotomy to intestinal bypass or resection satisfied these criteria. These included 245 patients diagnosed between the years mentioned above and 38 patients diagnosed before 1961. As the follow-up extends to the end of 1971, the period of follow-up ranges from 1 to 23 years. For analysis these patients have been classified into three groups according to the site or sites of initial bowel involvement as shown in *Table I*.

Table 1: SITE OF CROHN'S DISEASE AT INITIAL DIAGNOSIS

Group	Site of disease	No. of cases	%
1	Small bowel only	155	55
2	Ileocolitis	81	28
3	Large bowel only	47	17

Table II: INDICATIONS FOR INITIAL SURGERY

Indication	Small bowel (*n* = 155) %	Ileocolitis (*n* = 81) %	Large bowel (*n* = 47) %	Total (*n* = 283) %
Obstruction	35	25	4	27
Fistula	5	9	24	9
Severe alimentary symptoms	41	43	53	44
Suspected appendicitis	12	13	4	11
Failed medical treatment	7	10	15	9

Indications for initial surgical procedures and subsequent admissions

Initial surgery

The data in *Table II* classify the 283 patients according to what appeared to be the main indication for the initial surgical procedure. These may be resolved into those of an emergency nature for acute symptoms (66) and those of a more chronic nature leading to elective surgery (217).

Fifty-five of the 66 patients who had emergency surgery in their first attack proved to have chronic Crohn's disease confined to the small bowel and accounted for one-third of this whole group (group 1). The most frequent indication was a diagnosis of acute appendicitis or of intestinal obstruction. In the former case surgery was often confined to appendicectomy or drainage of an abscess; in the latter more definitive surgery for Crohn's disease was undertaken. In 6 cases a perforation of the distal ileum or caecum in association with chronic Crohn's disease was the cause of the acute presentation.

---

* Department of Surgery, Stobhill General Hospital, Glasgow. Present address of G. Gillespie: Victoria Infirmary, Glasgow.

Table III: INDICATIONS FOR SUBSEQUENT ADMISSIONS

Indication	Small bowel ($n = 99$) %	Ileocolitis ($n = 47$) %	Large bowel ($n = 29$) %	Total ($n = 175$) %
Obstruction	30	16	10	23
Fistula	20	29	24	23
Severe alimentary symptoms	38	45	62	44
Abscess	6	5	0	4
Anaemia/weight loss	6	5	4	6

Elective surgery was also performed to relieve patients with intestinal obstruction of a more subacute or chronic nature. Many of these patients had already had a trial period of medical treatment and the signs of obstruction merely precipitated surgery. Similarly, the presence of a fistula of the abdominal wall or in the perineum provided the immediate indication for a surgical procedure in 9 per cent. In 44 per cent with 'severe alimentary symptoms' operation was undertaken because of persisting abdominal pain, often associated with diarrhoea or weight loss (20 patients were suspected of having malignant disease), in the hope that a surgical procedure might be curative or relieve their more clamant symptoms.

In the remaining 9 per cent elective surgery was undertaken because these patients had become gastrointestinal cripples due to continued weight loss and diarrhoea in spite of apparently adequate conventional supportive medical treatment.

Subsequent admissions

Table III indicates the main reason for subsequent admissions which were followed by a period of supervised medical treatment or further surgery.

In each case a diagnosis of chronic Crohn's disease had already been made macroscopically or histologically, so that subsequent surgery, where necessary, was usually elective. The indications for surgery assumed a similar pattern, displaying little alteration in the proportions of patients showing signs of either intestinal obstruction or severe alimentary symptoms. There was, however, a marked rise both in the overall numbers and in the proportion of patients with fistula.

Surgical procedures

Three main types of surgery were used in the treatment of patients in this series, namely laparotomy/biopsy, bypass surgery and resection. This study was not prospectively planned and therefore patients undergoing each form of surgery were not deliberately matched. However, patients undergoing surgery for Crohn's disease in the more common sites (i.e. small bowel disease and ileocolitis), forming 83 per cent of the total series, were comparable for mean age, general condition and extent of disease, though a somewhat higher incidence of skip lesions was observed among patients undergoing resection. In the patients with lesions confined to the large bowel (17 per cent), although there was a preponderance of elderly females, there were likewise no differences among patients having each form of surgery.

Laparotomy

a. Small bowel lesions: Thirty patients with small bowel Crohn's lesions had laparotomy at the initial surgical procedure. Twenty-one patients (70 per cent) have already been readmitted with a major recurrence at a mean of 1 year later (6 months to 6 years), and 19 of these have required further operation (resection 12, bypass 7).

b. Crohn's ileocolitis: Ten patients had laparotomy and 4 had anal or rectal biopsy as the initial surgical procedure. Ten patients (71 per cent) have been readmitted with a major recurrence at a mean of 2 years later (3 months to 4 years), and 7 of these have required further surgery (laparotomy/biopsy 4, bypass 2, resection 1).

c. Large bowel lesions: Fifteen patients had confirmation of diagnosis either by laparotomy (2) or by anal or rectal biopsy (13) as the initial surgical procedure. Ten (66 per cent) have been readmitted with major recurrence at a mean of 1 year later (3 months to 2½ years), and 8 of these have required definitive surgery (bypass 5, resection 2, laparotomy/biopsy 1).

Bypass surgery

a. Small bowel lesions: Thirty-two patients had bypass in continuity as the initial surgical procedure. Nineteen (61 per cent) have been readmitted with a major recurrence at a mean of 5 years later (4 months to 26 years), and 18 of these required further surgery (resection 14, bypass 3, laparotomy/biopsy 1).

Six patients had bypass with exclusion as the initial surgery. No recurrences have so far been observed in a 1–5-year follow-up.

b. Crohn's ileocolitis: Nine patients had bypass in continuity as the initial surgical procedure. Eight patients (82 per cent) have since had a major recurrence of whom 4 have required further surgery (resection). Bypass with exclusion was the initial operation in 5 patients, of whom 2 have required further surgery (resection).

c. Large bowel lesions: Seven patients had colostomy without resection as the initial surgical procedure. Four (59 per cent) have been readmitted with a recurrence at a mean of 9 months later (4–20 months), and 3 of these required further surgery (resection).

Resection

a, Small bowel lesions: Eighty-seven patients had resection as the initial surgery. Thirty (37 per cent) patients have been readmitted with recurrence at a mean of 5 years later (3 months to 20 years), and 20 of these have required further surgery (resection 12, bypass 3, laparotomy/biopsy 5).

b. Crohn's ileocolitis: Fifty-three patients had resection as the initial procedure. Eighteen (34 per cent) patients have been readmitted with recurrence at a mean of 5 years later (1 month to 14 years), and of these, 14 have required further surgery (resection 8, laparotomy or biopsy 5, bypass 1).

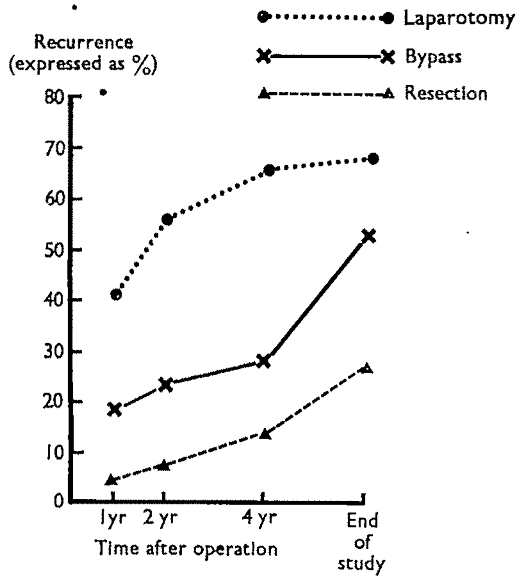


Fig. 1. Incidence and time of recurrence after surgery for small bowel Crohn's disease.

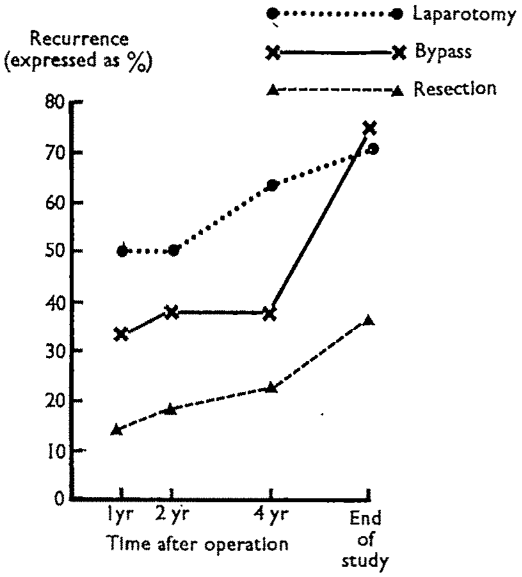


Fig. 2. Incidence and time of recurrence after surgery for Crohn's ileocolitis.

Table IV: RECURRENCE AFTER INITIAL SURGERY

Type of surgery	Small bowel %	Ileocolic %	Large bowel %
Laparotomy/biopsy	70	71	67
Bypass or colostomy	51	77	57
Resection	37	34	18

c. *Large bowel lesions*: Twenty-five patients had an elective resection as the initial surgical procedure. Four (18 per cent) have been readmitted with recurrence at a mean of 1 year later (3 months to 5 years), and 2 of these have required further surgery (resection).

By the end of 1971, 123 of 155 (80 per cent) patients with small bowel lesions had undergone one or more resections; 63 of 81 (77 per cent) patients with Crohn's ileocolitis and 33 of 47 (70 per cent) patients with large bowel lesions had likewise had one or more resections.

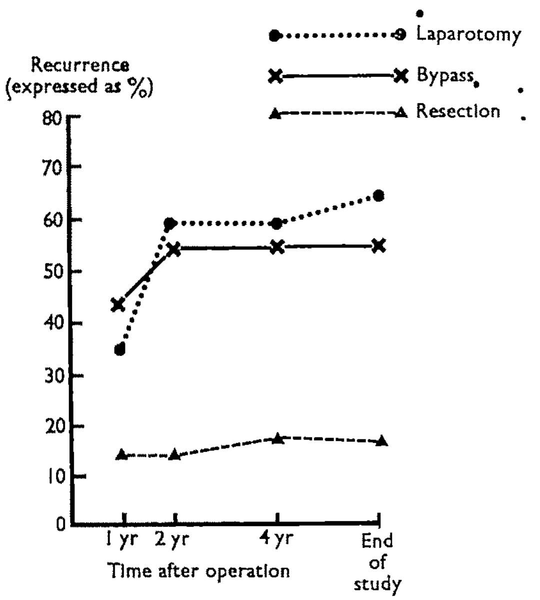


Fig. 3. Incidence and time of recurrence after surgery for large bowel Crohn's disease.

Recurrence after initial surgery

In this study a recurrence was defined as further major symptoms either resulting from recrudescence or complications of the disease at the original site or resulting from extension of the pathological process to involve other areas, proved by radiology, surgical operation or histology and requiring inpatient hospital stay. The follow-up period ranged from 1 to 26 years. The incidence of recurrence has been expressed as a percentage of the surviving patients in each category and is shown in *Table IV*.

The incidence of recurrence after exploratory laparotomy or bypass procedures is high for lesions in all sites. Following resection, however, recurrence is appreciably less common, especially for large bowel lesions.

Time of appearance of recurrences

The time at which recurrent disease occurs after the three main types of surgery is of interest and *Figs.* 1, 2 and 3 show the recurrences, expressed as percentages, which have occurred at 1, 2 and 4 years after surgery in patients with small bowel lesions, ileocolitis and large bowel lesions respectively. It is clear that by 4 years after laparotomy the number of recurrences for patients with small bowel lesions and ileocolitis has virtually reached the level observed at the end of the study period, and that this occurs even earlier at around 2 years when large bowel lesions are considered. However, it is noteworthy that at the same stage the incidence of recurrence after bypass surgery for patients with small bowel lesions and ileocolitis has only reached 50 per cent of the final observed recurrences at the end of the study.

Assessment of recurrences after secondary operations is only meaningful for further resections in patients with small bowel lesions since only this group contained adequate numbers for analysis. The recurrences at 1, 2 and 4 years showed a similar pattern to those seen after initial resection.

Postoperative complications

Perforation: Four patients had free perforations of bowel within 10 days of a surgical procedure. All occurred either in skip lesions or in segments of bowel involved by Crohn's disease but left *in situ* at the initial operation. One had jejunal perforation following a colonic resection; 2 patients had multiple perforations of ileum, in one case after laparotomy and in the other proximal to an anastomosis while continuing on steroid therapy; the fourth patient had free caecal perforation after more distal colonic resection and anastomosis.

Fistula formation: Thirty patients (11 per cent) developed an external fistula after operation. Twelve followed laparotomy with or without appendicectomy, 10 followed a bypass procedure and 8 followed resection.

Of the external fistulas occurring after laparotomy with or without appendicectomy, 8 followed drainage of an abscess in the right iliac fossa and 4 of these were proved to have arisen from diseased ileum, including the only case occurring after appendicectomy. Four of those occurring after bypass surgery were likewise shown to arise from diseased ileum.

Where surgical correction of the fistula was required, resection of the affected segment of bowel (18) and bypass with exclusion (1) were immediately successful. Three closed after excision of the track alone, but only after a long interval. Bypass in continuity was equally unpredictable, failing in 1 patient and succeeding in 2 after a delay of over 6 months. Gradual closure was obtained by using azothiaprine in 2 patients.

Anastomotic leakage: This occurred on 10 occasions and led to 9 postoperative deaths at an average of 12 days after surgery. All but one occurred after resection with end-to-end anastomosis. Four occurred after ileal resection, 3 after right hemicolectomy and 2 after left colon resection.

Postoperative mortality

Postoperative mortality refers to deaths within 28 days of surgery, performed during any admission. The 283 patients in this series had a total of 418 surgical procedures. There were 21 postoperative deaths. Ten of these resulted from anastomotic leakage after resection. Laparotomy was attended by a 7 per cent mortality, bypass surgery 2 per cent and resection 5 per cent.

There were 7 additional late related deaths; 2 from malabsorption, 2 from mesenteric vascular occlusion, 1 from sepsis, 1 from anaemia requiring transfusion and 1 from perforation of a gastric ulcer while on steroids. Ten late unrelated deaths occurred.

Extension of disease

At the time of initial diagnosis 55 per cent of patients had disease confined to the small bowel, 28 per cent had Crohn's ileocolitis and 17 per cent had disease confined to the large bowel. However, by the time of review at the end of the study period in 1971, only 47 per cent had disease confined to the small bowel, whereas 39 per cent had ileocolitis and 13 per cent had disease confined to the large bowel, indicating extension of the disease, most often into a more distal portion of the alimentary canal.

Discussion

Indications for surgery in Crohn's disease may be single or multiple, but in this review we have presented what we believe to have been the main indication both for the primary surgical procedures and for subsequent admissions with major symptoms. The most frequent indication for elective surgery in the present series was 'severe alimentary symptoms' (44 per cent), but if the patients who required surgery because of failure to respond to medical treatment (9 per cent) are included, then over 50 per cent of the present series came to surgery because of distressing alimentary symptoms or other uncontrolled medical problems. De Dombal et al. (1971a) also observed a preponderance of patients (81 per cent) requiring surgery for 'chronic disease'.

Many patients in this series who had varying degrees of intestinal obstruction also had other intestinal symptoms, but in such cases obstruction has been taken as the principal indication. It is of interest, therefore, that in the Glasgow region intestinal obstruction was the indication for initial surgery and for subsequent readmission in only 26 and 23 per cent of patients respectively. Similar findings of 20 and 30 per cent respectively have been reported from Leeds (de Dombal et al., 1971a). In the United States, however, the incidence of obstruction as the prime indication for initial surgery and for subsequent readmission appears to be much higher, for example 47 per cent (Barber et al., 1962) and 84 per cent (Colcock, 1964). The reasons for this discrepancy are not immediately obvious, although clearly a more prolonged conservative policy prior to initial surgery, as practised by Garlock (1967), would offer one possible explanation.

In this series the incidence of local peritonism from ileal or ileocolic Crohn's disease sufficient to mimic acute appendicitis was 11 per cent, though some workers have found a higher proportion presenting in this fashion (Atwell et al., 1965).

Of all the patients requiring their initial surgery as an emergency procedure in the present series 83 per cent were found to have Crohn's disease confined to the small bowel, and the finding of unsuspected and otherwise uncomplicated regional enteritis may often have influenced the surgeon towards a conservative surgical management.

External fistulae in the present series occurred in 9 per cent of patients prior to the initial surgery at which the diagnosis of Crohn's disease was established, but in almost all cases followed upon drainage of a local intra-abdominal abscess. Indeed, apart from a greater incidence of external fistulas subsequent to initial surgery, there was a marked similarity in the pattern of indications for initial surgery and for subsequent readmissions (*Tables II, III*). This observation highlights the fact that surgery may only provide a temporary respite from exacerbations in a disease which has a natural tendency to chronicity and recurrence.

Turning to the surgical management of Crohn's disease, it is clear that most workers in the past decade have advocated resection (Barber et al., 1963; Letwin et al., 1963; Atwell et al., 1965; Colcock and Fortin, 1965; de Dombal et al., 1971a; Kyle, 1971). In all of these studies, as in the present series, the conclusions are open to criticism in that the studies were retrospective and the operative procedures were not randomly allocated in a prospective manner. However, in the Glasgow series it appeared that the surgeons had exercised a free choice of surgical procedures since the incidence of patients with extensive or complicated local disease in each surgical group was low. It would seem reasonable, therefore, to make some general observations and comparisons of the surgical procedures used in the Glasgow study.

The present series appears to have a high incidence of exploratory operations without definitive surgery. This has occurred because many of these operations were performed for diagnostic reasons, or the Crohn's disease was discovered either at an emergency operation for suspected appendicitis or during elective surgery for other abdominal conditions. In such situations the surgeon avoided definitive surgery in apparently uncomplicated disease in which spontaneous remission is not unknown. Thus, these cases might reasonably be considered to reflect the natural history of the disease. Indeed, the findings of the present series show that a proportion of patients do remain free from major symptoms (30 per cent), but this figure may be even lower with a more extended follow-up. Seventy per cent of patients undergoing exploratory operation as the sole procedure have therefore had a major recurrence of symptoms requiring admission to hospital, and 60 per cent have required further surgery. These findings accord well with the report by Edwards (1969) and may support a more aggressive approach to Crohn's disease discovered at laparotomy.

Bypass in continuity offers a simpler technical procedure although recurrence rates of between 40 and 92 per cent are quoted (Williams, 1971). This experience is borne out by the Glasgow study where 67 per cent of patients having an initial bypass in continuity required further admission on account of major recurrence of symptoms. Bypass with exclusion, a procedure relatively neglected in this series, has been advocated on the grounds of a lower recurrence rate. Although not without its own rare hazards of perforation associated with closed loop obstruction (Waye and Lithgoe, 1967; Steinberg et al., 1973a, b) and intussusception (Garlock, 1967), it does seem a procedure worthy of further evaluation.

Resection, on the other hand, has in this series been followed by the lowest recurrence rate (33 per cent), and this agrees well with the experience of other large series (37 per cent Colcock, 1964; 34 per cent de Dombal et al., 1971b). Recurrence is commoner after ileal disease (37 per cent) and ileocolic disease (34 per cent) than after large bowel disease alone (18 per cent), and this supports the findings of others (Marshak et al., 1966; de Dombal et al., 1971a). Examination of the recurrence rate following bypass surgery and purely exploratory procedures shows little difference. The question then arises as to whether bypass surgery alters the natural history of the disease or offers any respite from symptoms. Examination of the rate of recurrence up to 4 years after surgery clearly shows that the recurrence rate in the early period after bypass surgery is approximately half that seen following an exploratory procedure when small bowel disease (group 1) and ileocolic disease (group 2) are considered. In these groups of patients it is clear that bypass surgery does prolong the period of remission for a large number of patients. However, for patients with large bowel disease alone (group 3) no advantage was conferred by colostomy as the sole procedure, and this procedure should be reserved for obstructive lesions. On the other hand, the recurrence rate up to 4 years after resection is much lower in all three groups, but since recurrence is related to length of follow-up (Garlock et al., 1951; de Dombal et al., 1971b; Fielding et al., 1972), this procedure may only have postponed the occurrence of major symptoms for a considerable number of patients. The presence of distant skip lesions untouched but recognized at resection of the principal diseased segment may also adversely affect the results of excisional surgery. Nevertheless, on the basis of the 4-year postoperative results, it seems clear that resection offers the best prospects as regards risk of recurrence.

Any assessment of the relative merits of surgical procedures must of course be influenced by the postoperative morbidity and mortality. External fistulas after initial surgery occurred not uncommonly and in the present series provided the indication for readmission in 23 per cent of cases (19 per cent Schofield, 1965; 21 per cent Koutny, 1968; 19 per cent Edwards, 1969). Fistulation was more frequent after laparotomy (18 per cent) or bypass operation (12 per cent) where the diseased bowel remained *in situ* than after resection (3 per cent). The Birmingham series (Steinberg et al., 1973a, b) gave closely similar figures (19, 13 and 5 per cent respectively). In the Glasgow series there were, in addition to the 6 free perforations prior to initial surgery, 4 free perforations within 10 days of operation, none of which was adjacent to an anastomosis. Nevertheless, free anastomotic leakage occurred on 10 occasions in the series and all but one followed resection. With one exception, anastomotic leakage proved fatal.

The immediate postoperative mortality in the present series was 7·4 per cent, although the overall death rate from causes directly related to Crohn's disease was 9·9 per cent. This mortality rate is remarkably similar to that reported in other large European series. De Dombal (1972) reported an overall death rate from causes related to Crohn's disease of 11·3 per cent with a postoperative mortality of 7·2 per cent. Davis (1961) reported a 9 per cent death rate from causes related to Crohn's disease. While there may be an irreducible mortality for surgery in this disease, Kyle (1973) has suggested that 'proper and timely' resection may carry a mortality of only 2 per cent. It seems likely that incomplete resection of involved bowel may explain some of the 5 per cent of deaths following resection in the Glasgow series by making anastomotic leakage or perforation more likely, and this reflects the surgeon's difficulty in making a macroscopic assessment at operation of the extent of disease (Atwell et al., 1965). Furthermore, these postoperative problems may reflect the natural instinct of the surgeon in resecting to a minimal extent in a disorder where the likelihood of further surgery is high.

Indeed the tendency for the disease to extend or recur proved one of the prominent features of this study, and it is noteworthy that a large number of patients who initially had disease confined to the small bowel (group 1) later developed ileocolitis (group 2) due to progression of the disease. This tendency for extension to occur in an aboral manner has been previously noted for large bowel disease alone (Brahme and Wenckert, 1970), but so far has received little attention in small bowel disease.

Perhaps it is no longer the place of surgery in the management of Crohn's disease which requires evaluation but the timing of operation. As to which procedure is best, final proof may have to await prospectively planned studies.

Acknowledgements

We wish to thank the surgeons of the West of Scotland Surgical Association for permission to study the records of their patients. Thanks are also due to the record staffs of all the hospitals in the Glasgow region for help, to the Medical Illustrations Department of the Victoria Infirmary, Glasgow, for the figures and to Mrs Anne Whyte and Miss Patricia Leask, Victoria Infirmary, for secretarial help. Finally, we are most grateful to Sir Andrew Watt Kay, Regius Professor of Surgery, Western Infirmary, Glasgow, for helpful guidance in preparing the final manuscript.

References

ATWELL J. D., DUTHIE H. L. and GOLIGHER J. C. (1965) The outcome of Crohn's disease. *Br. J. Surg.* **52**, 966–972.

BARBER K. W., WAUGH J. M., BEAHRS O. H. and SAUER W. G. (1962) Indications for and the results of surgical treatment of regional enteritis. *Ann. Surg.* **156**, 472–482.

BARBER K. W., WAUGH J. M. and SAUER W. G. (1963) Surgical treatment of complications of regional enteritis. A 10 year follow-up. *Arch. Surg.* **86**, 442–444.

BANKS B. M., ZETZEL L. and RICHTER H. S. (1969) Morbidity and mortality in regional enteritis. *Am. J. Dig. Dis.* **14**, 369–379.

BRAHME F. and WENCKERT A. (1970) Spread of lesions in Crohn's disease of the colon. *Gut* **11**, 576–584.

COLCOCK B. P. (1964) Regional enteritis: a surgical enigma. *Surg. Clin. North Am.* **44**, 779–784.

COLCOCK B. P. (1967) Surgical treatment of regional enteritis. *Am. J. Surg.* **114**, 398–401.

COLCOCK B. P. and FORTIN C. (1965) Surgical treatment of regional enteritis. *Ann. Surg.* **161**, 812–818.

DAVIS J. M. (1961) The prognosis of Crohn's disease of the small intestine. *Postgrad. Med. J.* **37**, 783–791.

DE DOMBAL F. T. (1972) Surgical treatment for Crohn's disease. *Gut* **59**, 826–829.

DE DOMBAL F. T., BURTON I., CLAMP S. E. and GOLIGHER J. C. (1974) Short term course and prognosis of Crohn's disease. *Gut* **15**, 435–443.

DE DOMBAL F. T., BURTON I. and GOLIGHER J. C. (1971a) The early and late results of surgical treatment for Crohn's disease. *Br. J. Surg.* **58**, 805–816.

DE DOMBAL F. T., BURTON I. and GOLIGHER J. C. (1971b) Recurrence of Crohn's disease after primary excisional surgery. *Gut* **12**, 519–527.

EDWARDS H. (1969) Crohn's disease: an enquiry into its nature and consequences. *Ann. R. Coll. Surg. Engl.* **44**, 121–139.

FAHRLANDER H. and BAERLOCHER C. (1971) Clinical features and epidemiological data on Crohn's disease in the Basle area. *Scand. J. Gastroenterol.* **6**, 657–662.

FIELDING J. F., COOKE W. T. and WILLIAMS J. A. (1972) The incidence of recurrence in Crohn's disease. *Surg. Gynecol. Obstet.* **134**, 467–469.

GARLOCK J. H. (1967) *Current Surgical Management* London, Saunders, pp. 184–188.

GARLOCK J. H., CROHN B. B., KLEIN S. H. and YARNIS M. (1951) An appraisal of the long term results of surgical treatment of regional ileitis. *Gastroenterology* **19**, 414–423.

JONES J. H., LENNARD-JONES J. E. and LOCKHART-MUMMERY H. E. (1966) Experience in the treatment of Crohn's disease of the large intestine. *Gut* **7**, 445–452.

KOUTNY J. (1968) Expérience clinique et chirurgicale dans 70 cas de maladie de Crohn. *Acta Chir. Belg.* **67**, 981–1010.

KYLE J. (1971) An epidemiological study of Crohn's disease in north-east Scotland. *Gastroenterology* **61**, 826–833.

KYLE J. (1973) *Crohn's Disease*. London, Heinemann, p. 201.

LETWIN E., BONDAR G. F. and MACKENZIE W. C. (1963) Crohn's disease, diagnosis and management of 50 surgically proven cases. *Can. J. Surg.* **6**, 450–455.

MARSHAK R. H., LINDNER A. E. and JANOWITZ M. D. (1966) Granulomatous ileocolitis. *Gut* **7**, 258–264.

MORSON B. C. (1971) Histopathology of Crohn's disease. *Scand. J. Gastroenterol.* **6**, 573–575.

NORLEN B. J., KRAUSE U. and BERGMEN L. (1970) An epidemiological study of Crohn's disease. *Scand. J. Gastroenterol.* **5**, 385–390.

SCHOFIELD P. F. (1965) The natural history and treatment of Crohn's disease. *Ann. R. Coll. Surg. Engl.* **36**, 258–279.

SLANEY G. (1968) Crohn's disease. *Br. Med. J.* **3**, 294–298.

SMITH I. S., YOUNG S., GILLESPIE G., O'CONNOR J. and BELL R. (1975) Crohn's disease in Clydesdale: epidemiological aspects. *Gut* **16**, 62–67.

STEINBERG D. M., COOKE W. T. and WILLIAMS J. A. (1973a) Free perforation in Crohn's disease. *Gut* **14**, 187–190.

STEINBERG D. M., COOKE W. T. and WILLIAMS J. A. (1973b) Abscess and fistulae in Crohn's disease. *Gut* **14**, 865–869.

WAYE J. D. and LITHGOE, C. (1967) Small bowel perforation in regional enteritis. *Gastroenterology* **53**, 625–629.

WILLIAMS J. A. (1971) The place of surgery in Crohn's disease. *Gut* **12**, 739–749.

ANNUAL SUBSCRIPTION, Vol. 63 (1976)

The publishers regret that, because of rising production and dispatch costs, a further increase in the subscription rate has proved unavoidable. The annual subscription to the *British Journal of Surgery* for Volume 63 (1976) will be £22·50 (single copies £2·00).

Significance of faecoliths in the diagnosis of acute appendicitis

B. GILL AND R. E. CUDMORE*

SUMMARY

Three cases are presented which demonstrate the significance of faecoliths in the diagnosis of acute appendicitis in infants. A wide spectrum of symptoms is noteworthy. The usefulness of a plain X-ray of the abdomen in infants with acute abdomen is stressed.

ACUTE appendicitis is probably the most common surgical emergency encountered in a children's hospital. The diagnosis is usually made on clinical judgement alone because it is well known that ancillary investigation may be misleading. Routine radiography of the abdomen is rarely helpful except to indicate intestinal obstruction. In an ill infant, however, where the diagnosis of appendicitis may be uncertain, X-ray of the abdomen may show a faecolith. Should it do so, the diagnosis of appendicitis is certain.

Case reports

Case 1: M. M., an 8-week-old male infant was admitted to Alder Hey Children's Hospital, Liverpool, on 31 August 1973 with a history of refusing feeds, vomiting and mild upper respiratory infection for 3 days. He was febrile, lethargic, dehydrated and had slight abdominal distension and tenderness in the right iliac fossa. An erect X-ray of the abdomen showed multiple fluid levels and a faecolith in the right iliac fossa.

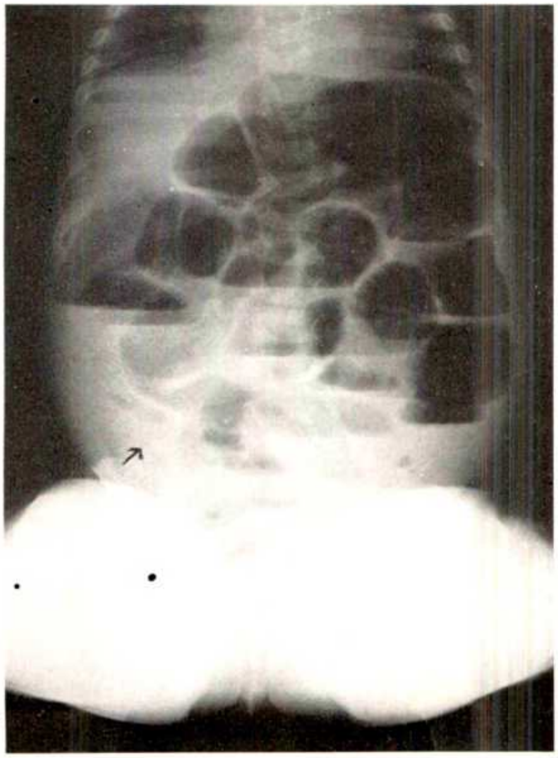


Fig. 1. *Case* 2. Erect film of the abdomen showing distended loops of small bowel with fluid levels and a round faecolith in the right iliac fossa.

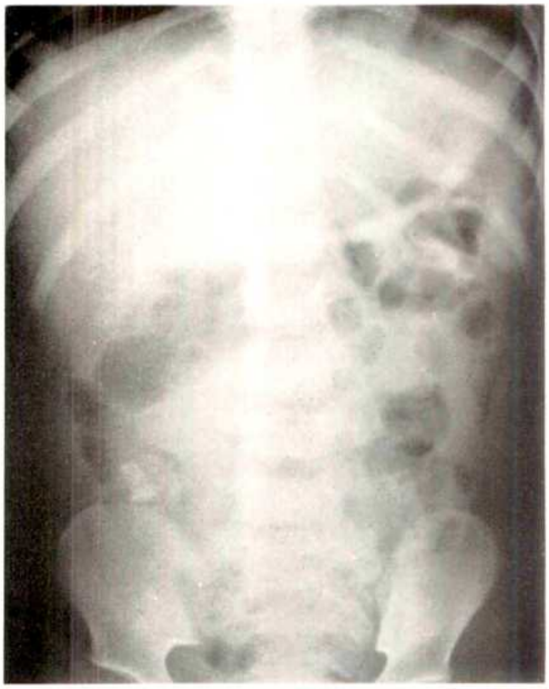


Fig. 2. *Case* 3. X-ray of the abdomen showing no evidence of obstruction, but a large rectangular faecolith in the right iliac fossa.

Through a right lower quadrant muscle-cutting incision a perforated gangrenous appendix was removed and the wound drained. Postoperatively he was treated with an intravenous infusion, gastric suction and wide spectrum antibiotics. Ten days later he developed right upper lobe collapse, which required a second course of antibiotics. He made good progress and was discharged after 4 weeks.

Case 2: C. D., a 21-month-old male was admitted on 31 October 1973 having been febrile, lethargic and refusing feeds for 4–5 days. There had been no diarrhoea or upper respiratory infection and he had vomited only once. He was a sick infant with a poor peripheral circulation. The most remarkable features were gross abdominal distension, oedema and tenderness on the right side of the abdomen and absent bowel sounds. An X-ray of the abdomen showed the features of an adynamic ileus and a faecolith in the right iliac fossa (*Fig.* 1).

After initial resuscitation with intravenous fluids and antibiotic therapy a perforated gangrenous appendix was removed. The faecolith lay free in the peritoneal cavity. The peritoneum

---

* Paediatric Surgical Unit, Alder Hey Children's Hospital, Liverpool.

was drained and the wound closed. Distension persisted for 3 days, followed by diarrhoea and spontaneous decompression. The wound dehisced on the tenth day and was resutured. Recovery after this was uneventful. He was discharged after 3 weeks.

Case 3: A. B., a 1-year-old female, was admitted on 26 March 1974, with a history of being generally unwell with anorexia, vomiting and fever for 48 hours. On admission her temperature was 39 °C. A proper physical examination required sedation with Vallergan. She was noted to have tenderness and guarding in the right iliac fossa and was reluctant to move her right leg. An erect film of the abdomen showed fluid levels and a large faecolith in the right iliac fossa (*Fig.* 2). A perforated gangrenous appendix was removed and the peritoneal cavity drained. Recovery was slow but uneventful. She was discharged after 3 weeks.

Discussion

Appendicitis in children under 2 years is very rare. Snyder and Chaffin (1952) and Wilkinson et al. (1969) reported an incidence of less than 2 per cent. Grosfield et al. (1973) discussed in great detail the clinical features, management and the pitfalls in the diagnosis of acute appendicitis in the first 2 years of life. Our 3 cases illustrate almost all the clinical signs described by them, with one additional common feature—that of a faecolith in the right iliac fossa, demonstrable on an erect X-ray film of the abdomen (*see Figs.* 1 and 2). Wilkinson et al. (1969) described the X-ray features in the diagnosis of appendicitis in infants and reported a faecolith in 33 per cent of his cases. Grosfield et al. (1973) reported an incidence of 28 per cent which is much higher than the 10 per cent reported in older children and the 7 per cent in adults (Brooks and Killen, 1965).

Appendicitis, for all its masquerading in the early years of life, should be considered a curable condition. There has been a tremendous reduction in mortality, but it is still as high as 6·7 per cent (Fields and Cole, 1967) and 9·3 per cent (Crosfield et al., 1973), presumably because of a high perforation rate due to late diagnosis.

From the above results one concludes that in this age group a plain X-ray of abdomen should form an essential part of the investigation of the sick infant with possible abdominal pathology. Where a faecolith is shown the diagnosis is certain and early exploration is mandatory.

Addendum

Since this article was submitted for publication there have been a further 3 cases with similar clinical and radiographic findings who were shown to have appendicitis.

References

BROOKS D. W. jun. and KILLEN D. A. (1965) Roentgenographic findings in acute appendicitis. *Surgery* **57**, 377–384.

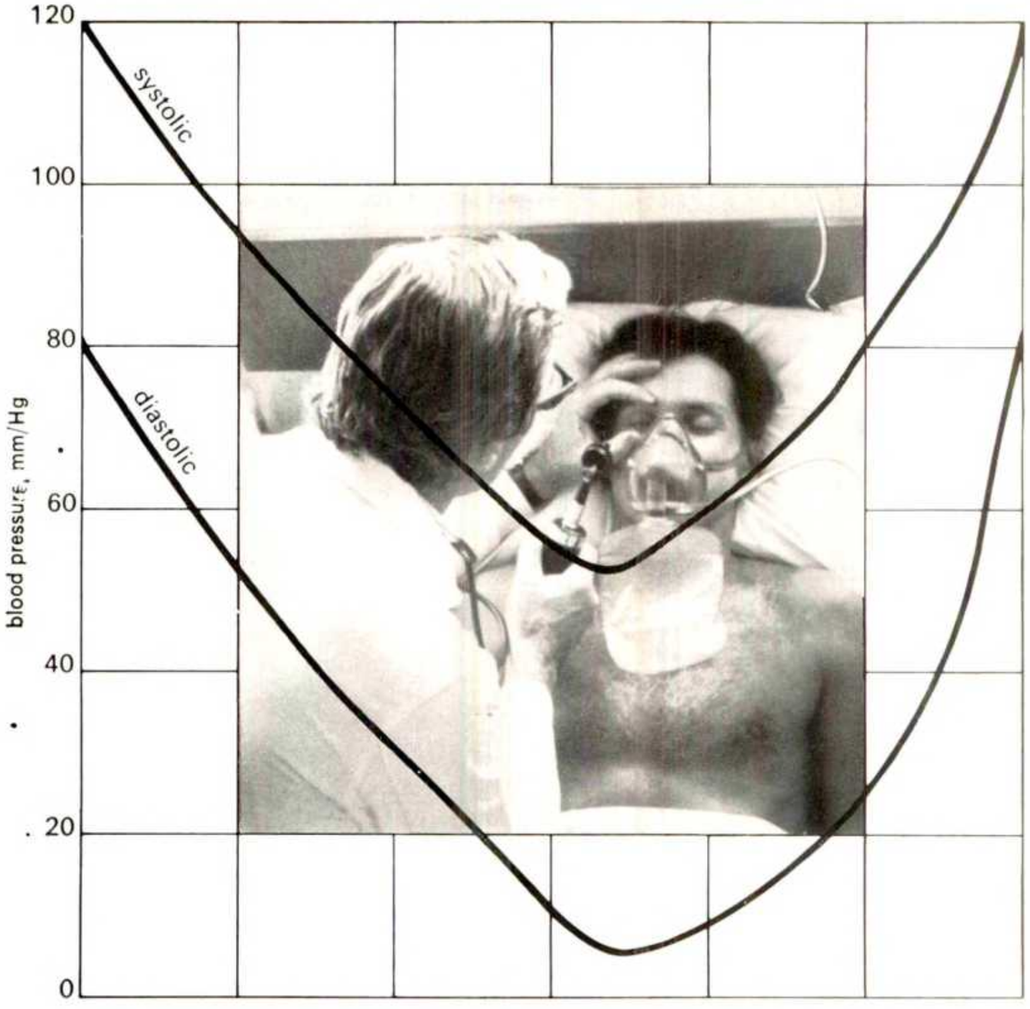
GROSFIELD J. L., WERNBERGER M. and CLATWORTHY H. W. jun. (1973) Acute appendicitis in the first two years of life. *J. Pediatr. Surg.* **8**, 285–293.

FIELDS I. A. and COLE N. M. (1967) Acute appendicitis in infants 36 months of age or younger. *Am. J. Surg.* **113**, 269–275.

SNYDER W. H. jun. and CHAFFIN L. (1952) Appendicitis in the first two years of life. *Arch. Surg.* **64**, 549–560.

WILKINSON R. H., BARTLETT R. H. and ERAKLIS A. J. (1969) Diagnosis of appendicitis in infancy: the value of abdominal radiographs. *Am. J. Dis. Child.* **118**, 687–690.

Survival rate in shock can be increased with massive doses of corticosteroids



Injection DECADRON® Shock-Pak

Dexamethasone sodium phosphate/MSD

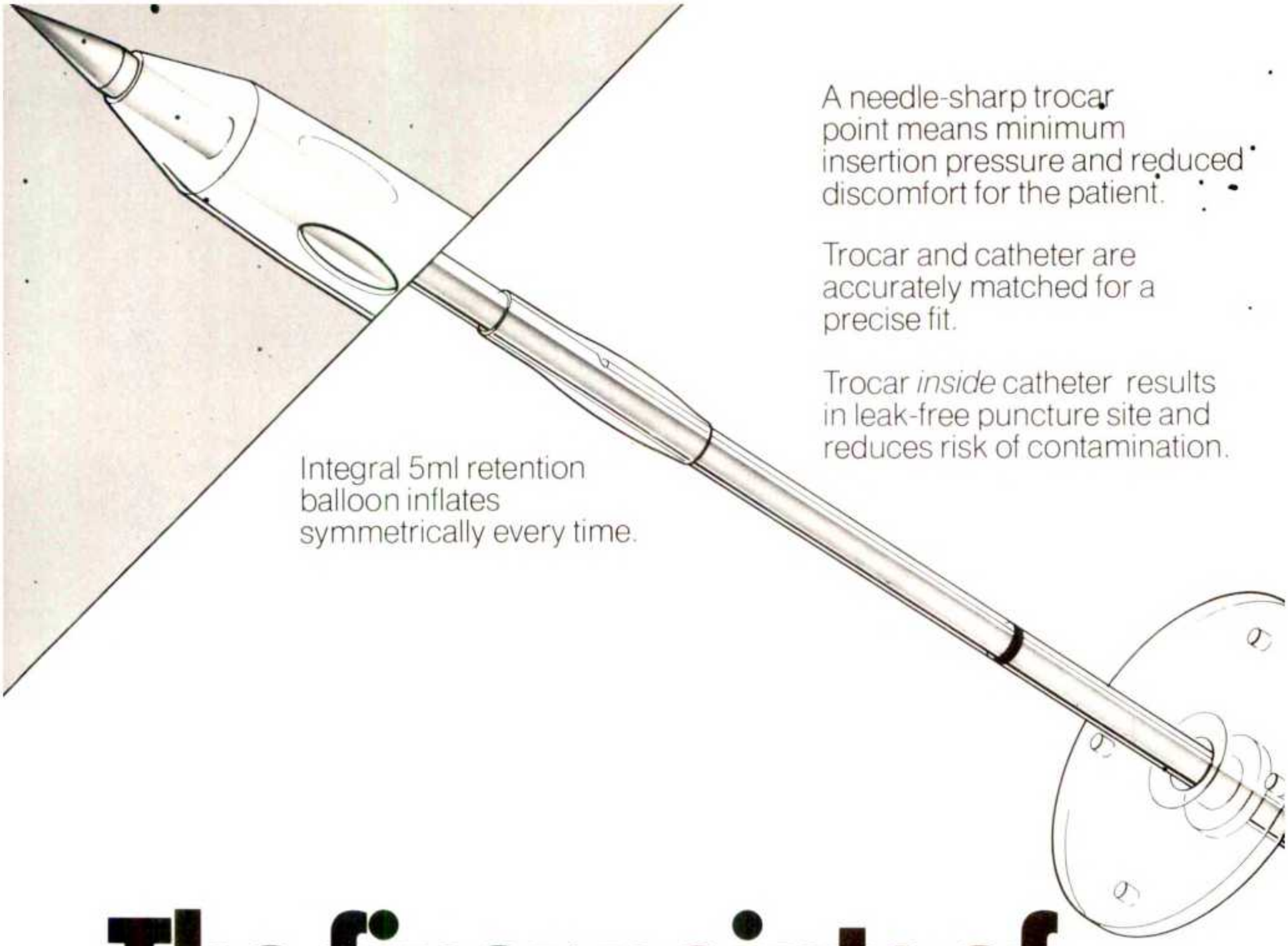
20 mg/ml (new strength)

In severe shock, treatment with Injection 'Decadron' Shock-Pak is an adjunct to, and not a substitute for, specific or supportive measures that the patient may require, e.g. restoration of circulating blood volume, correction of fluid and electrolyte balance, oxygen, surgical measures, and antibiotics.

Supplied in 5 ml ampoules containing per ml, dexamethasone sodium phosphate equivalent to 20 mg dexamethasone. Detailed information is available to physicians on request. ® denotes registered trademark.

Merck Sharp & Dohme Limited
Hoddesdon, Hertfordshire. Telephone Hoddesdon 67123

5-2920 (IMC)



A needle-sharp trocar point means minimum insertion pressure and reduced discomfort for the patient.

Trocar and catheter are accurately matched for a precise fit.

Trocar *inside* catheter results in leak-free puncture site and reduces risk of contamination.

Integral 5ml retention balloon inflates symmetrically every time.

The finer points of a suprapubic catheter.

Our precisely engineered trocar and catheter combines maximum efficiency in operation with ease of use.

Check these points and see for yourself.

Sherwood MEDICAL INDUSTRIES

Sherwood Medical Industries Limited. London Road. County Oak. Crawley. West Sussex RH10 2T

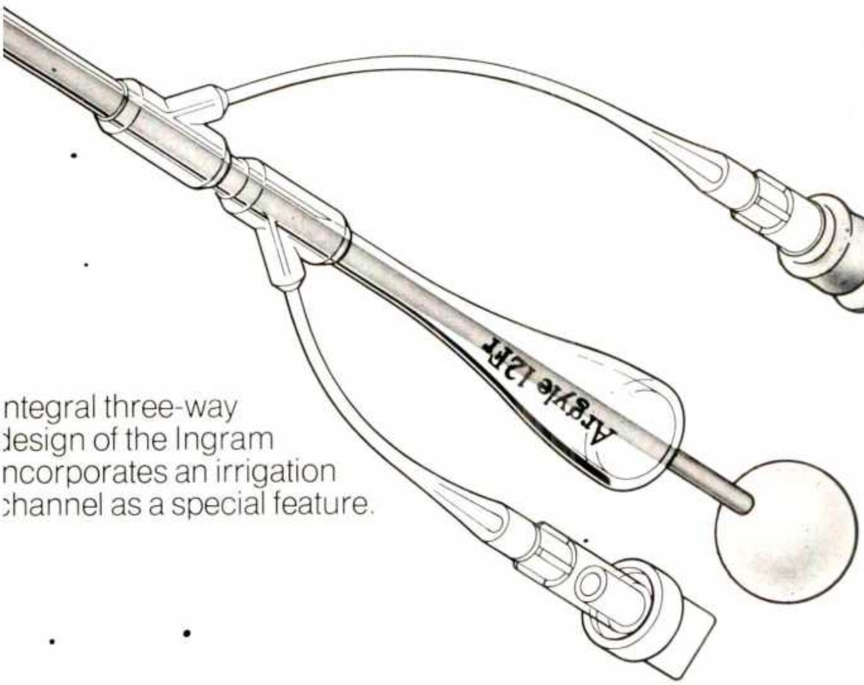
Tip, bevel, eyes. All ultra-smooth, all designed to minimise tissue damage.

Exclusive X-ray opaque Sentinel Line and Eye assists accurate location and positioning of catheter.

Available in both 12Ch and 16Ch sizes. Each unit packed in a convenient peel-back sterile tray.

liding plastic collar enables
atheter to be firmly
xed to maintain position.

nflation channel located inside
he catheter wall. Drainage lumen
is therefore unobstructed.



ntegral three-way
esign of the Ingram
ncorporates an irrigation
hannel as a special feature.

OR SAFE, EFFICIENT
RINARY DRAINAGE

ARGYLE
INGRAM TROCAR CATHETER

THE ARGYLE INGRAM TROCAR CATHETER
Please send me full technical literature ☐
Ask your representative to call ☐
ame BLOCK CAPITALS PLEASE
ddress
ignature

Nolvadex–a more acceptable approach to breast cancer treatment

Drug therapy is often both uncomfortable and distressing for the patient with advanced breast cancer. But now a more acceptable treatment is available for such patients, 'Nolvadex' (tamoxifen).

'Nolvadex' is an oestrogen antagonist. Whilst it is just as effective as other treatments, it has no hormonal properties. Virilization–common with androgens–is unknown; oedema, nausea and vomiting occur much less frequently than with oestrogens.

'Nolvadex' is taken as twice-daily oral doses. So treatment is simple as well as more acceptable.

Further information–including the results of U.K. trials with 'Nolvadex'[1,2] is available on request.
References: 1 *British Journal of Cancer* (1971), 25, 270.
2 *British Medical Journal* (1973), 1, 13.

ICI Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

THE QUEEN'S AWARD TO INDUSTRY 1966 1967 1968 1969 1970 1972

Nolvadex
Easier to give, easier to take
'Nolvadex' is a trade mark

Br. J. Surg. Vol. 62 (1975) 537–541

The changing pattern of hospital admissions for diverticular disease of the colon

JAMES KYLE AND ALAN I. DAVIDSON*

SUMMARY

Hospital admissions for symptomatic diverticular disease of the colon were studied during two periods, 1958–61 and 1968–71, in a relatively closed community in north-east Scotland. There was a significant increase in the numbers admitted, from 206 to 366. In the earlier 4-year period among patients aged 70 years and over there was a preponderance of females, but in the later study period the risk of developing symptomatic disease was almost as great among elderly males. Most of the elderly female patients were widowed city dwellers. The proportion of patients requiring operation for or dying from diverticular disease declined, but perforation remained as a frequent complication carrying a high mortality.

In the early years of this century diverticular disease of the colon was rare (Keith, 1910). At that time males were affected more often than females. The male to female ratio in Leeds was 2 : 1 (Telling and Gruner, 1917). The introduction of barium enema examinations (de Quervain, 1914; Spriggs and Marxer, 1927) made recognition easier, and the diagnosis of diverticular disease was made more frequently. The symptomatic forms of the disease are known to be very much commoner in Europeans than in Africans, Asians or Melanesians (Wells, 1949; Kyle et al., 1967; Painter and Burkitt, 1971). However, no detailed investigation has been conducted in a relatively static European community to ascertain whether or not there has been any change in the numbers of patients with troublesome disease who require to be admitted to hospital, or any alteration in the severity of the disease and the need for surgical intervention. The present study was undertaken in order to provide this information.

The north-east of Scotland is a region particularly suitable for this type of comparative study. Geographically, it is relatively isolated from the rest of Scotland, its hospital services are centralized in Aberdeen and until the end of 1971 there had been very little change in the population of the region.

Patients and methods

Records were obtained of all the patients in north-east Scotland who required admission to hospital because of symptomatic colonic diverticular disease during two study periods 10 years apart. The periods were each of 4 years' duration, from 1958 to 1961 and from 1968 to 1971 respectively. The same methods of ascertainment and evaluation, and the same diagnostic criteria were used throughout the two periods. The population figures were based on the 1961 and 1971 censuses (Registrar General, 1963, 1973), which showed that the population of the area had fallen from 393 801 to 389 610.

Ascertainment

Since 1955 all general hospital records in the area have been centralized, being coded and stored in the Records Department of the Royal Infirmary, Aberdeen. Retrieval of records from this department has proved to be remarkably accurate (Kyle, 1971), and the Records Department provided the case sheets of all the patients admitted during the study periods. In addition, all morbid anatomy in the area is carried out in the University Department of Pathology, which supplied information about resected specimens and autopsies on patients with diverticular disease.

Diagnostic criteria

Only patients having colonic diverticular disease as their principal reason for admission to hospital were accepted. The presence of diverticula was confirmed by barium enema, by operation or at autopsy in every case. In addition each patient had at least two of the following clinical features: (*a*) left-sided or lower abdominal pain; (*b*) deep tenderness in the left iliac fossa; (*c*) altered bowel habit; (*d*) rectal bleeding; (*e*) pyrexia over 37·5 °C; (*f*) leucocytosis of 10 000/mm^3 (10^9/l) or more.

Geographical limits

The patients were permanently resident within the city of Aberdeen and the counties of Aberdeenshire, Banff and Kincardine. The three hospitals where diverticular disease is investigated and treated are all in Aberdeen. Some suburban districts, market towns and fishing ports are included with the mainly rural areas of the counties.

Exclusions

1. Patients in whom diverticular disease was an incidental finding; these were mostly long stay geriatric patients with other serious illnesses.
2. Solitary diverticulum of the caecum, which may be congenital.
3. Unexplained rectal bleeding where diverticula had not been convincingly demonstrated.

The number of hospital patients of each sex and the corresponding admission rates were calculated, and the change between the two study periods was then

---

* Gastroenterological Research Unit, Royal Infirmary, Aberdeen.

Table I: CHANGE IN ADMISSIONS FOR COLONIC DIVERTICULAR DISEASE IN NORTH-EAST SCOTLAND

Sex	No. of admissions 1958–61	1968–71	Increase (%)
Males	74	139	87
Females	132	227	72
Total	206	366	77

Table II: POPULATION OF NORTH-EAST SCOTLAND AGED 30 YEARS AND OVER IN 20-YEAR AGE GROUPS

Age group	1961 Male	1961 Female	1971 Male	1971 Female
30–49	47 370	52 225	43 925	47 265
50–69	30 873	48 814	40 440	48 090
70–89	11 029	17 808	12 240	19 851

Table III: MALE PATIENTS WITH DIVERTICULAR DISEASE OF THE COLON

Age group	No. of patients 1958–61	No. of patients 1968–71	Admission rates† 1958–61	Admission rates† 1968–71	Increase in rates‡
30–49	4	12	2·1	6·8	×3·2*
50–69	46	59	28·8	36·5	×1·3
70–89	24	66	54·4	134·8	×2·5*
30–89	74	137	18·8	35·5	×1·9*

† Hospital admission rate per 100 000 population per year.
‡ Rate in 1968–71 expressed as a proportion of the rate in 1958–61.
* Significant at 5 per cent level.

Table IV: FEMALES WITH SYMPTOMATIC COLONIC DIVERTICULAR DISEASE

Age group	No. of patients 1958–61	No. of patients 1968–71	Admission rates† 1958–61	Admission rates† 1968–71	Increase in rates‡
30–49	3	13	1·4	6·9	×4·9*
50–69	53	83	17·1	43·1	×1·6*
70–89	76	126	106·7	158·7	×1·5*
30–89	132	222	27·8	48·3	×1·7*

† Hospital admission rate per 100 000 population per year.
‡ Rate in 1968–71 expressed as a proportion of the rate in 1958–61.
*Significant at 5 per cent level.

Table V: RATIO OF ADMISSION RATES

Age	Male : female admission rates 1958–61	1968–71
30–49	1·50	0·99
50–69	1·06	0·85
70–89	0·51	0·85

analysed statistically. The incidence of major complications, the need for elective surgery and the mortality for the two 4-year periods were compared.

Results

Hospital admissions

During the first period, 1958–61, 206 patients with colonic diverticular disease were admitted to hospital, compared with 366 in the second period, 1968–71 (*Table I*). The annual hospital admission rates per 100 000 population were, therefore, 12·8 and 23·5 respectively.

The age of the patients in the two periods was very similar, ranging from 35 to 89 years in the first period and from 32 to 95 years in the second. No case was encountered in the first three decades of life, and the population at risk was aged 30 years and above. *Table II* shows this population broken down into 20-year age groups. Between 1968 and 1971 there were 2 males and 5 females aged 90 years or more. These are excluded from *Tables III* and *IV*, which show the numbers of male and of female patients in each of three 20-year age groups admitted in the two study periods, together with the corresponding hospital admission rates per 100 000 of the population at risk. The increases in the admission rates between 1958–61 and 1968–71 are given. Apart from middle-aged males, the increases in cases admitted were statistically significant at the 5 per cent level for the three age groups of both sexes.

Between 1958 and 1961 there were 74 males and 132 females, while for 1968–71 the corresponding figures were 139 and 227 respectively. The totals for both sexes increased between the two periods, but the increase was proportionately greater for males than for females. In the earlier study there was a male preponderance of nearly 3 : 2 in the 30–49 age group, but a 2 : 1 female preponderance beyond the age of 70 years. In the second study this marked swing with advancing years had vanished, the male to female ratio approximating to 1 : 1 for each of the three 20-year age groups (*Table V*).

Elective operations

Table VI shows the number of elective operations performed. Staged elective procedures have been counted as single operations. Although the number of patients admitted had increased by almost 80 per cent, the actual numbers of operations considered necessary were almost identical in the two periods. Consequently, the percentage of patients coming to operation in 1968–71 declined.

Complications

Colovesical fistula is perhaps the most dramatic complication of colonic diverticular disease. The number of cases noted was 5 in the first period and 4 in the second. However, perforation is potentially the most lethal complication. The number of colonic perforations rose from 18 in the 1958–61 period to 28 in 1968–71, an increase that closely parallels that in the hospital admissions for diverticular disease. The mortality rate for perforation also rose from 28 to 39 per cent.

Mortality

Twenty-five patients (7 male, 18 female) in the first period and 26 patients (9 male, 17 female) in the second study period died as a direct result of their diverticular condition. The mortality rate fell from 12·1 to 7·1 per cent.

Discussion

The distinction formerly made between 'diverticulosis' and 'diverticulitis' has been abandoned. Resected specimens of colon from patients who clinically appeared to have had diverticulitis may not show any evidence of inflammation on histological examination (Morson, 1963). Radiological appearances which at one time were considered to be helpful in differentiating diverticulosis from diverticulitis are now known to be unreliable (Parks et al., 1970). Consequently, the term 'diverticular disease of the colon' is preferred. In the present investigation all the patients were having symptoms from their disease, the symptoms being judged sufficiently severe to merit admission to hospital. This has not been the case in previously published series, many of which contained both inpatients and outpatients. Diagnostic criteria frequently were different or were not stated and often geographical limits and the size of the populations at risk were undefined. Direct comparison of the present results with those from earlier series is therefore impossible. The Aberdeen hospital admissions for the two study periods 10 years apart have simply been compared with each other. All the patients in the area rely on the hospitals in Aberdeen for medical services, and no patients go to other centres for treatment.

Elective operations are undertaken only after careful consideration, and it was felt that comparison of the numbers performed in the two periods might be relevant. By contrast, emergency procedures are employed for so many different complications that analysis would not be meaningful. Only two clear-cut and unmistakable complications, perforation and colovesical fistula, have been studied. Other complications such as obstruction (Bolt, 1973) and rectal haemorrhage (Heald and Ray, 1971) have many possible causes and may vary greatly in severity, and consequently they have not been considered.

The marked increase in hospital admissions in the Aberdeen area during a decade is statistically significant. Does it represent a true change in the incidence of diverticular disease in a community that was relatively closed until the end of 1971? The criteria for acceptance into each of the two study groups were applied uniformly by the same observers. The proportion of case records rejected was very similar on both occasions—131 excluded and 206 accepted for the 1958–61 period, 261 excluded and 366 accepted for 1968–71. The exclusions mostly were cases where either the diagnosis was presumptive but not proved or the demonstrated diverticula of colon were considered to be incidental findings, not responsible for admission to hospital. The diagnostic methods in use were identical throughout; colonoscopy was not used before 1971. The increase in hospital admissions therefore seems genuine, but this increase in the hospital admission rate for severe disease does not necessarily mean that the incidence of colonic diverticula in the population at risk has also risen. However, from the surgeon's point of view the admission rate is the best guide that is available as to how common potentially troublesome diverticula are in the community. It is clearly impractical to subject large numbers of apparently normal people to repeated barium enema examinations.

There may be several explanations for the larger numbers admitted, apart from a true increase in incidence. First, the level of diagnostic activity may have risen, particularly with regard to radiological investigation. It is true that the number of barium enema examinations carried out at Aberdeen Royal Infirmary rose from 892 in 1960 to 1800 in 1971, although this need not imply that twice as many patients with diverticula in their colons were found. Fifteen years ago patients with real bowel symptoms and abdominal pain almost certainly would have had a barium enema. In more recent times, contrast examinations may frequently have been requested in order to exclude a somewhat unlikely lesion rather than in the reasonable expectation of finding it. Only 20–25 per cent of patients in whom diverticular disease is demonstrated need to come into hospital. An independent radiological survey in this area (Petrie et al., 1972) for the 4 years 1967–70 revealed 1567 cases with major diverticula formation in the colon, but in 1968–71 only 366 patients required admission. A similar observation has been made in New York (Gennaro and Rosemond, 1974). Part of the increase in the number of barium enemas could well be due to more patients really developing diverticula and requiring X-ray, even if the proportion admitted remained constant.

A second possible explanation for the increased number of hospital cases is that the criteria for admission have changed. A patient in genuine distress would have been admitted at once in any of the years studied, but it is possible that with an ageing population in recent years more elderly people were admitted for investigation rather than for active treatment. About 40 per cent of patients with colonic diverticular disease have other major associated illnesses (Kyle, 1968), and during 1968–71 some patients in this category may have been admitted for a few nights rather than having a barium enema performed as an outpatient. It seems likely that there has been a slight but important change in the surgeon's indications for ordering a barium enema and in the decision as to whether it should be performed on an inpatient or an outpatient basis.

An increase in the age of the population could contribute to the larger number of inpatients with diverticular disease. The older a person is, the more likely is he or she to have diverticula (Manousos et al., 1967). Above the age of 70 years about 40 per cent of the population have the condition; at this stage of life asymptomatic diverticula should probably be regarded as a variant of the normal rather than a pathological abnormality. Between 1961 and 1971 there was an 11 per cent increase in the population group aged between 70 and 89 years, the increase being nearly twice as great for females (2053) as for males (1211). Clearly, if 40 per cent of these additional elderly citizens developed diverticula, and if 20 per cent of those so affected required admission to hospital, the extra 160 patients in 1968–71 are readily accounted for. Unfortunately, this simple theory does not explain the disproportionate rise in the number of

Table VI: ELECTIVE OPERATIONS FOR COLONIC DIVERTICULAR DISEASE

Date	Male No.	Male %	Female No.	Female %
1958–61	13 (74)	18	18 (132)	4
1968–71	16 (139)	12	18 (227)	9

Numbers in parentheses are the total numbers of patients of each sex for the study period.

male patients in the second study period, when the population change showed twice as many additional females as males in the 70–89-year age group. Nevertheless, the gradual ageing of the population at risk must be a major factor in accounting for the observed changes in the admission rates for diverticular disease in north-east Scotland.

The similarity in the numbers of elective operations and of deaths in the two study periods might suggest that indeed the pattern of diverticular disease had not changed, and that only the willingness to admit to hospital had altered. However, between the two study periods very important changes in treatment were introduced. In 1964 Painter advocated the high residue diet for medical treatment, and Reilly described the operation of colomyotomy. The high residue diet has been of great value in clinical practice and could well account for the observed reduction in the percentage of patients requiring operation shown in *Table VI*. Mortality expressed as a percentage of the total number of cases might also be expected to fall with better methods of treatment. It is not considered that the actual numbers of operations and deaths indicate that the numbers admitted are falsely high.

Colovesical fistula is probably the outcome of severe and long-standing diverticular disease. With improved medical treatment the chances of any individual patient developing this complication should be reduced, and this appeared to be true in 1968–71. The complication which increased markedly was perforation into the peritoneal cavity. The number of perforations rose by 61 per cent between 1958–61 and 1968–71; this percentage increase was broadly similar to that for admissions (77 per cent), and so tends to support the accuracy of the latter figure. Certainly the diagnosis of perforation was not being made too readily in the second study period—the mortality for perforation rose from 28 per cent to a disconcerting 39 per cent. Perhaps too much reliance should not be placed on the rising number of perforations of the colon, because in diverticular disease it may behave in maverick fashion, sometimes striking out of the blue and occasionally affecting younger subjects.

There is no ready explanation for the changing sex pattern in diverticular disease of the colon. The findings in the earlier part of this investigation are in agreement with those reported from Belfast (Parks, 1969), a slight excess of males below 50 years of age changing to a marked excess of female patients aged over 70 years. In the second part of the present investigation the chances of a male in any of the three 20-year age groups at risk developing symptomatic disease were almost as great as for a female. In studying the 1968–71 case records it became apparent that a disproportionately large number of the females lived in the City of Aberdeen—128 out of 227 (56·4 per cent) compared with 54 out of 139 males (39·2 per cent). Only 46·7 per cent of the total population of the area reside within the city. Among the female city patients 83 (61·2 per cent) were 70 years of age or over, the majority being widowed; 24 male city patients (44·4 per cent) were in this age group. However, diverticula do not develop overnight, and the place of residence at the time of admission is much less important than the place where the patient spent the major part of his or her life.

Acknowledgements

We thank Miss I. Dingwall-Fordyce, Department of Community Medicine, and Mr G. Hems, Department of Statistics, University of Aberdeen, for their help with the statistical analyses, and Mrs J. Amonoo and Miss M. Paterson for secretarial assistance.

References

BOLT D. E. (1973) Diverticular disease of the large intestine. *Ann. R. Coll. Surg. Engl.* **53**, 237–245.

GENNARO A. R. and ROSEMOND G. P. (1974) Diverticulitis of the colon. *Dis. Colon Rectum* **17**, 74–78.

HEALD R. J. and RAY J. E. (1971) Bleeding from diverticula of the colon. *Dis. Colon Rectum* **14**, 420–427.

KEITH A. (1910) Diverticula of the alimentary tract of congenital or of obscure origin. *Br. Med. J.* **1**, 376–380.

KYLE J. (1968) Prognosis in diverticulitis. *J. R. Coll. Surg. Edinb.* **13**, 136–141.

KYLE J. (1971) An epidemiological study of Crohn's disease in north east Scotland. *Gastroenterology* **61**, 826–833.

KYLE J., ADESOLA A. O., TINCKLER L. F. and DE BEAUX J. (1967) Incidence of diverticulitis. *Scand. J. Gastroenterol.* **2**, 77–80.

MANOUSOS O. N., TRUELOVE S. C. and LUMSDEN K. (1967) Prevalence of colonic diverticulosis in general population of Oxford area. *Br. Med. J.* **3**, 762–763.

MORSON B. C. (1963) The muscle abnormality in diverticular disease of the colon. *Proc. R. Soc. Med* **56**, 798–800.

PAINTER N. S. (1964) The aetiology of diverticulosis of the colon with special reference to the action of certain drugs on the behaviour of the colon. *Ann. R. Coll. Surg. Engl.* **34**, 98–119.

PAINTER N. S. and BURKITT D. P. (1971) Diverticular disease of the colon: a deficiency disease of Western civilization. *Br. Med. J.* **2**, 450–454.

PARKS T. G. (1969) Natural history of diverticular disease of the colon: a review of 521 cases. *Br. Med. J.* **4**, 639–642.

PARKS T. G., CONNELL A. M., GOUGH A. D. and COLE J. Y. (1970) Limitations of radiology in the differentiation of diverticulitis and diverticulosis of the colon. *Br. Med. J.* **2**, 136–138.

PETRIE J. C., NEEDHAM C. D. and GILLANDERS L. A. (1972) Survey of alimentary radiology findings in the north east of Scotland region (1967–70). *Br. Med. J.* **2**, 78–80.

DE QUERVAIN F. (1914) Zur Diagnose der erdwordvenen Didedarmdivertikel und der Symoidites diverticularis. *Dtsch. Z. Chir.* **128**, 67–85.

REGISTRAR GENERAL (1963) *Census 1961, County Reports.* London, HMSO.

REGISTRAR GENERAL (1973) *Census 1971, County Reports.* London, HMSO.

REILLY M. (1964) Sigmoid myotomy. *Proc. R. Soc. Med.* **57**, 556–557.

SPRIGGS E. I. and MARXER O. A. (1927) Multiple diverticula of the colon. *Lancet* **1**, 1067–1074.

TELLING M. W. H. and GRUNER O. C. (1917) Acquired diverticula, diverticulitis and peridiverticulitis of the large intestine. *Br. J. Surg.* **4**, 468–530.

WELLS C. A. (1949) Diverticula of the colon. *Br. J. Radiol.* **22**, 449–458.

Br. J. Surg. Vol. 62 (1975) 542–552

The nature of haemorrhoids*

W. H. F. THOMSON†

SUMMARY

An anatomical and clinical study aimed at uncovering factors likely to be helpful in understanding the true nature of haemorrhoids is described. The main finding was of specialized 'cushions' of submucosal tissue lining the anal canal; it is argued that piles are merely the result of their displacement.

THE theory that haemorrhoids result from varicosity of the anal submucosal veins, although currently orthodox, is not the only one available nor has it always been the most popular. In the past century, in fact, most European authorities considered piles to be caused by some sort of vascular tissue hyperplasia—a concept which recent work in Germany seems to support. Another theory suggests that piles are caused simply by a downward displacement of the anal canal lining. The three theories will now be reviewed.

The varicose vein theory

Dating from the time of Galen and Hippocrates (Parks, 1955), this theory probably stems from the observation of discrete dilatations on the course of the veins within the tissues of a haemorrhoid—John Hunter noticed them in a specimen that he dissected and clearly thought them to be the cause of haemorrhoids (Hunterian Museum (1848) *Descriptive Catalogue*).

The dilatations being thought of as the basic pathological change, various explanations were put forward to account for their development. There are two main groups: (1) explanations incriminating a localized increase in venous pressure, and (2) explanations incriminating a localized weakness in the vein wall.

The various mechanisms suggested as bringing about an increase in venous pressure are based on certain anatomical observations; the absence of valves in the portal vein and its tributaries, and the degree and site of the communications between the portal and systemic circulations in the anal canal. Morgagni (1749) introduced the idea that localization of the 'varices' to the anus might be attributable to the upright posture of man (the effect of the hydrostatic pressure resulting from an uninterrupted column of blood), and agreed with Boerhaave that the increased intra-abdominal pressure of straining would be transmitted to the anal veins. Verneuil (1855b), after injecting and dissecting the superior rectal vein and failing to find communications between it and the systemic circulation, suggested that the dilatations might be the result of obstruction to the venous return at the point where he had found the veins to pass through unprotected muscular 'button-holes' in the rectal wall (he thought the success of forcible dilatation of the anus—which he had introduced empirically in the treatment of piles—to be due to stretching of the 'button-holes' (Allingham and Allingham, 1896). Duret (1877) made similar dissections but discovered communications between the two systems traversing the anal sphincter. He therefore thought the fault lay in venous obstruction due to anal sphincter spasm and suggested a mechanism whereby the venous return upwards would also be cut off during defaecation.

Because none of the ideas of Morgagni, Verneuil or Duret seemed to explain the curious localization of the 'varices' to the lower half of the anal canal, Parks (1956) and later Graham-Stewart (1963) put forward alternative theories (although based on Duret's description of the anatomy) which seemed more adequately to fit the facts. However, free communications between the portal and systemic circulations in the anal canal have been demonstrated by Cruveilheir (1867), Konstantinowitch (1872), Quénu (1892) and Tuttle (1906) and so the concept that a localized increase in venous pressure is to blame in haemorrhoids is based on uncertain anatomical evidence.

Quénu, recognizing the lack of an anatomical mechanism to mediate a local increase in venous pressure, suggested that the fault lay in a weakness in the vein wall. He suggested that the venous dilatations, which he called 'haemorrhoids in miniature' (Quénu and Hartmann, 1895; *Fig.* 1), might be a manifestation of vein wall destruction brought about by recurrent infections resulting from repeated minor trauma at defaecation. He recognized, however, that there was little histological evidence to back up his ideas and his theory was never generally accepted. Recently, in fact, Jackson and Robertson (1965) reported that they had found no evidence of past or current infection in the haemorrhoidectomy specimens they had examined over the course of 2 years.

From this brief history the varicose vein theory can be seen to depend upon the observation of venous dilatations in the tissues of piles. However, Sappey (1874), Duret (1877) and Waldeyer (1899) have all reported finding dilatations on the course of the anal canal veins in children, suggesting that they are normal structures.

The vascular hyperplasia theory

Popular in the nineteenth century—Malgaigne (1837), Velpeau (1826), Bourgery (1840) and Cruveilhier (1852) considering piles to result from a sort of erectile tissue metaplasia, and Virchow (1863) and Allingham (1973) considering them to be haemangiomatous in nature—this theory probably arose out of the observed similarity between the tissues of a pile and cavernous tissue (Hunter, 1728–1793).

---

* The subject of a thesis accepted by London University for a Master of Surgery degree, 1974.

† Southampton General Hospital. Present address: Gloucester Royal Hospital.

The special nature of the anal submucosa, which Bourgery (1840) likened to an 'erectile web' and which Treitz (1853) noticed to be extraordinarily thick, was considered by Stieve (1928) to function as part of the anal continence mechanism by contributing to anal closure. Staubesand et al. (1963) demonstrated arteriovenous communications in the anal submucosa which seemed to them to indicate that the anal submucosa (which they also likened to cavernous tissue and called the 'corpus cavernosum recti') might have erectile properties; if so it would enhance, they believed, its capacity to fulfil its supposed function. Their observations stimulated them and Stelzner (1963) to suggest that piles might result from hyperplasia of the 'corpus cavernosum recti'. They cited in support the bright red colour of the bleeding (explicable, if coming from the venous spaces, on the basis of the existence of arteriovenous communications) and the fact that the bleeding of piles is said to be their earliest manifestation.

The sliding anal lining theory

Gass and Adams (1950) considered piles to result from degeneration of supportive tissue in the anal canal because of their observation, in 200 haemorrhoidectomy specimens, of fragmentation of connective tissue, and their belief that haemorrhoids were associated with a lax anus. Hughes (1957) and Patey (1972) supported the idea because it fitted the appearance of piles.

Of relevance is the existence in the anal submucosa of a substantial layer of smooth muscle. It was first described by Treitz (1853), who noted that it arose partly from the internal sphincter and partly, by passing through the internal sphincter, from the conjoined longitudinal muscle. He described it as passing downwards in the anal submucosa to form a supporting scaffold around the veins of the haemorrhoidal venous plexus and as making a significant contribution to the bulk of the columns of Morgagni. He considered it to function in preventing prolapse of the bulky tissues of the anal lining. Kohlrausch (1854), in describing it, expressed a similar view and called it the 'sustentator tunicae mucosae'. Ellis also discovered it in 1854 (Ellis and Ford, 1867) and, ignorant of the other two reports, called it the 'corrugator cutis ani'. Béraud (1858) next reported it, and later still, Roux (1881). Finally, it was described by Fine and Lawes (1940) who called it the 'muscularis submucosi ani'. For the sake of brevity and in recognition of his original discovery it will be called here 'Treitz's muscle'. Despite its repeated documentation it has yet to find a proper place in modern textbooks of anatomy.

The following investigation was undertaken in order to examine the premisses upon which the three hypotheses are based.

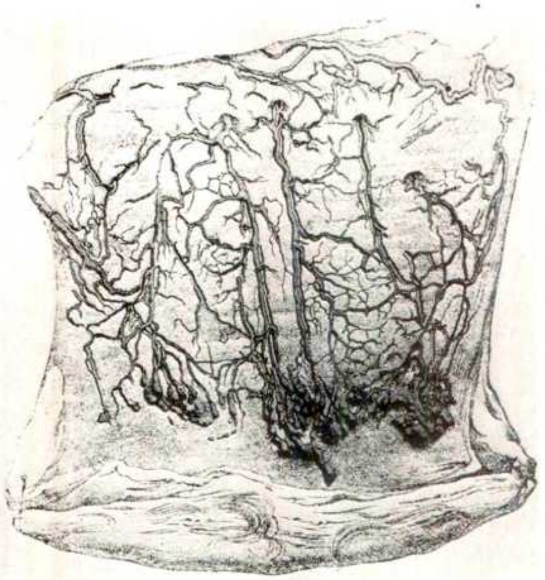


Fig. 1. Diagram from Quénu and Hartmann's (1895) *Chirurgie du Rectum*, showing the haemorrhoidal venous plexus after injection and dissection. The appearance of the venous dilatations, which they thought to be pathological, seems to have given rise to the term 'bunches of grapes' in connection with haemorrhoids.

Materials and methods

The study was partly anatomical and partly clinical.

The anatomical study

Ninety-five cadaveric anorectal specimens (obtained by pelvic exenteration *en bloc* with the anal canal from 10 infants, 3 adolescents and 82 adults) were prepared and dissected. Proctoscopy, with photography to provide a record, was carried out in 42 patients without haemorrhoids.

Demonstration of the arterial system: Fifty adult specimens were used. Each was prepared by injecting the superior rectal artery with latex and slitting the specimen open in the anterior midline. The entire extrarectal and submucosal course of the superior, middle and inferior rectal arteries (the parts incorporated in the specimen) was then dissected and a diagram made from each dissection.

Demonstration of the venous system: Fifty adult, 3 adolescent and 10 infant specimens were used. In 25 of the adult specimens the superior rectal vein was injected with a barium sulphate suspension and the specimen was slit open anteriorly and X-rayed. In the other 25 latex was injected and the venous system was dissected.

The 10 infant and 3 adolescent specimens were prepared in a different way. First, the superior rectal vein was cannulated and injected retrogradely with diluted ammoniated latex (Tompsett, 1970)—before removal of the specimen in order to facilitate cannulation (manipulation during removal usually empties the vein, which in infants then becomes invisible). Next the specimen was removed and the anorectum was slit open anteriorly. The anal canal lining, in

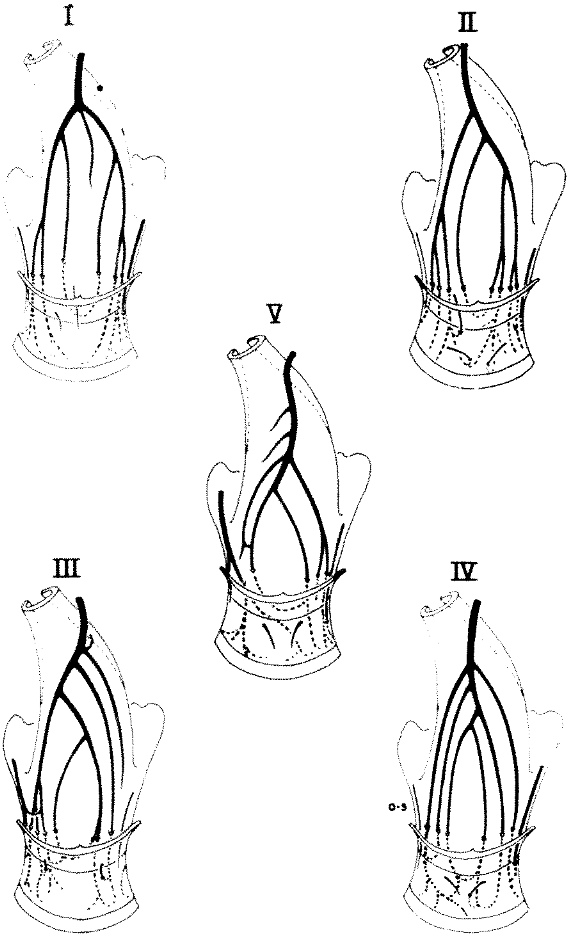


Fig. 2. Diagrams of the posterior aspect of dissected anorectal specimens showing five different patterns of arterial supply. The extrarectal course is represented by a continuous line and the submucosal by a dotted one. The middle rectal arteries can be seen joining the specimens anterolaterally above the levatores ani, and the inferior rectal vessels below the muscle, mainly posteromedially.

continuity with a cuff of perianal skin, was then dissected off the internal sphincter and subcutaneous part of the external sphincter and pinned out in formalin. After fixation it was rendered translucent by Spalteholz's technique (Culling, 1963) and studied under the dissecting microscope.

Demonstration of the arteriovenous communications: An anorectal specimen removed from the corpse of a young man soon after death was prepared. Infusion with saline through cannulae in both the superior rectal artery and vein enabled all severed vessels to be detected and sealed and the vascular tree to be cleared of blood. On completion (when perfusion of the superior rectal artery resulted in an almost clear flow from the vein) simultaneous infusion of the artery and vein was carried out using diluted ammoniated and filtered latex at constant pressure (red latex at 200 mm Hg and blue latex at 80 mm Hg respectively). The anal canal lining was then removed, rendered translucent as before and studied under the dissecting microscope.

Demonstration of Treitz's muscle: Treitz's muscle was demonstrated both macroscopically and microscopically. It was seen with the naked eye on raising the flap of anal lining as described above. Thirty-five specimens, slit open anteriorly, were dissected in the following manner; the perianal skin was dissected off the ischiorectal fat and external sphincter and, working cephalad, off the lowermost part of the internal sphincter; the muscle was then seen as a continuous layer of longitudinally running fibres on the deep surface of the flap. Further dissection showed it to arise circumferentially from the deep surface of the internal sphincter in almost discrete bundles which passed downwards into the anal submucosa and which had to be divided in order to elevate the flap. The appearance was recorded photographically.

For its microscopic demonstration longitudinal and transverse sections were made of the anal canal. In order to demonstrate its relationship to the venous plexus the veins were first distended by injecting the superior rectal vein with a mixture of barium sulphate and 4 per cent gelatin.

Demonstration of the anal 'cushions': This term, introduced for the first time, is used here to describe cushions of submucosal tissue in the anal canal. They were first observed during the proctoscopic examination of 42 consecutive patients with neither symptoms nor signs of haemorrhoids, and subsequently demonstrated in the anatomical preparations. The completely dissected flap of anal canal lining described above was merely held up to the light; discrete masses of thickened submucosa could then be clearly seen. They were demonstrated in 35 consecutive specimens—25 from adults and 10 from infants. Prior injection of the venous plexus made the cushions more obvious.

Proctoscopic examination of normal controls was carried out in the hope that it might provide information to explain the regular appearance of piles in the right anterior, right posterior and left lateral positions in the anal canal (Goodsall and Miles, 1900). It became clear that the anal lumen was not a simple anteroposterior slit as usually described (Phillips and Edwards, 1965) but a basically triradiate one. The appearance of the anal lumen in 42 normal patients was recorded photographically.

The clinical study

Eighty consecutive patients admitted to Southampton General Hospital for the surgical treatment of their prolapsing piles were asked which of their symptoms had started first, the bleeding or the prolapse. At operation the position and appearance of the piles were recorded by colour photography. The haemorrhoidectomy specimens were studied histologically.

Results

The anatomical study

The arterial system: Miles (1919) wrote that the branching pattern of the superior rectal artery was constant, being characterized by a bifurcation of the

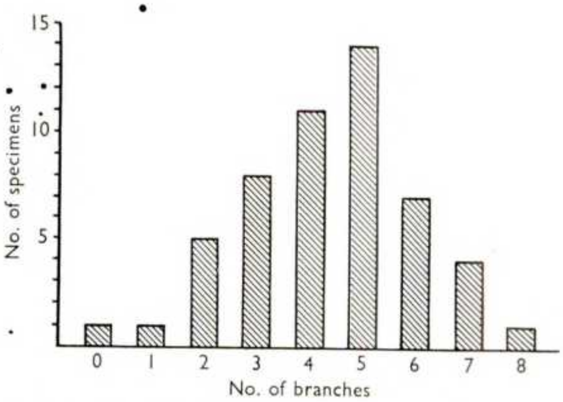


Fig. 3. Number of branches of the superior rectal artery reaching the haemorrhoidal zone.

main trunk into right and left branches with the right branch then producing anterior and posterior divisions while the left remained substantially single. He stated that it thereby determined the position of piles around the anal circumference (accounting for their regular appearance in the right anterior, right posterior and left lateral positions)—piles being said to be due to varicosity of the radicles of the superior rectal vein which, he said, followed the branches of the artery. However, Miles's description would not have been applicable to any of the 50 specimens which the present author has dissected, despite there being a wide variety of branching patterns amongst them (*Fig.* 2). In 23 specimens (46 per cent) the pattern was found to conform to the orthodox description (Warwick and Williams, 1973), the main trunk birfurcating to produce right and left divisions which then divided into a variable number of branches supplying the ipsilateral side of the rectum and anal canal; in the other 27 specimens various patterns were found. In some the main trunk passed to the right, giving off branches to the left, in others it passed to the left, supplying branches to the right, and in another group there was a trifurcation of the main trunk. The trifurcation group was also not uniform since the central component behaved in a number of different ways—supplying branches to both sides of the anal canal in some, to one side only in others and in yet others not reaching the anal canal, supplying only the rectum. Furthermore, the arrangement of the branches as they pierced the wall of the rectum to pass down into the anal submucosa was found to be unrelated to the primary branching pattern of the superior rectal artery; it was not unusual, in fact, to find a large primary branch being spent entirely in the supply of the rectum, not reaching the anal submucosa at all.

An average of five branches of the superior rectal artery was found actually to reach the haemorrhoidal zone (*Fig.* 3). However, in 35 specimens (70 per cent) substantial branches of one or both middle rectal arteries could also be traced into the anal submucosa, and in 21 specimens (42 per cent) the inferior haemorrhoidal arteries were found to make a similar contribution.

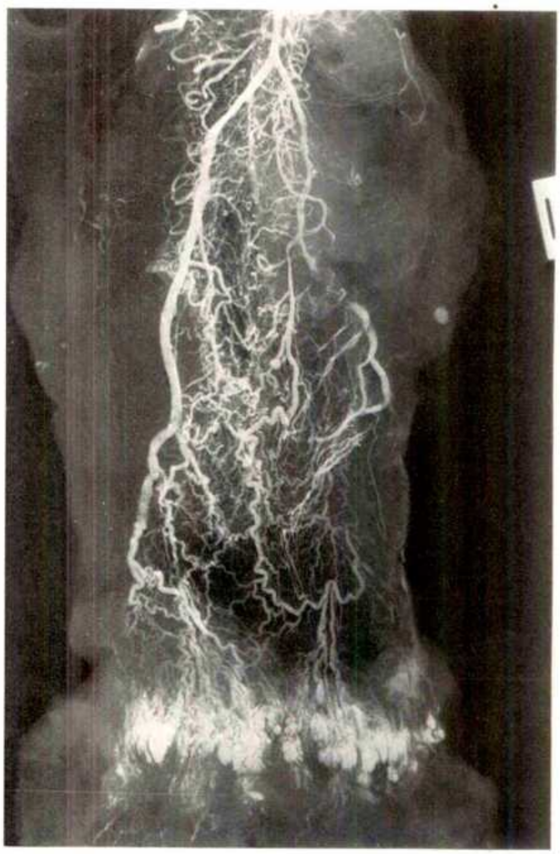


Fig. 4. X-ray of an opened-out anorectal specimen in which the superior rectal vein has been injected with a barium sulphate suspension. There was no evidence of piles; in other specimens where gross pile formations were present the radiographic appearance was the same.

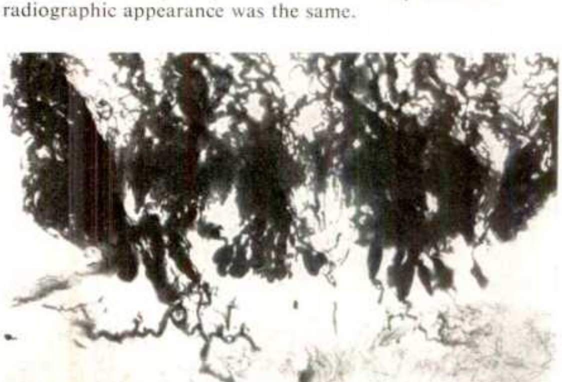
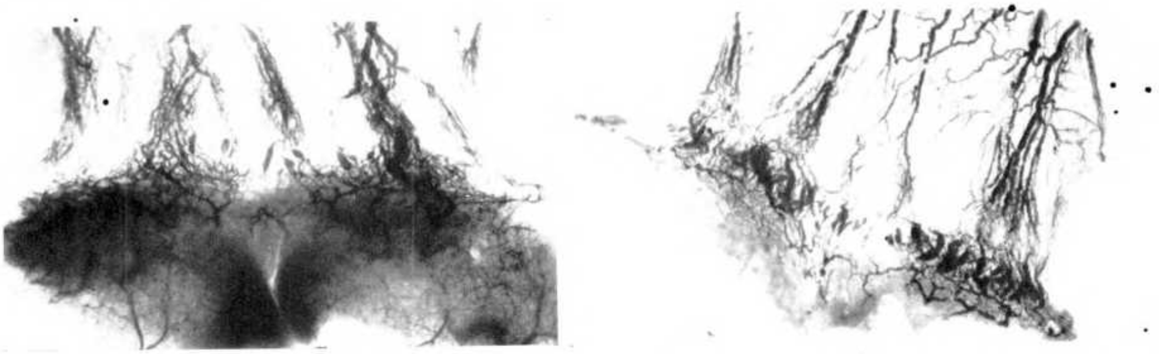


Fig. 5. Adult anorectal specimen prepared by latex injection of the superior rectal vein, followed by Spalteholz's procedure to render the tissues translucent; specimen slit open anteriorly.

In 5 specimens (10 per cent) an interesting and previously undescribed vascular anomaly was encountered, the middle rectal artery usurping, in the supply of the anal canal, part (and in 1 specimen, all) of the function of the superior rectal artery. Instead of piercing the muscle wall low down anteriorly as is usual (below the attachment of the levator ani at the



a

b

Fig. 6. Anorectal specimens from a full-term neonate (*a*) and a 3-month old infant (*b*). The superior rectal vein had been injected with coloured latex and the tissues cleared by Spalteholz's technique.

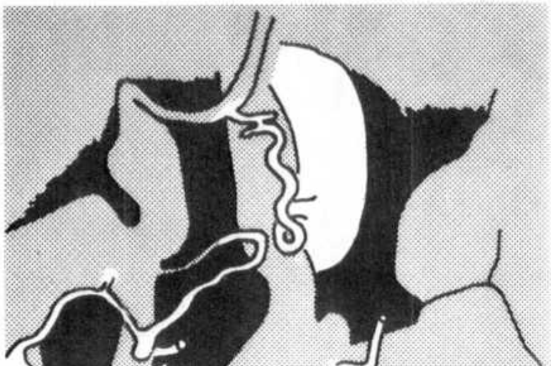


Fig. 7. A projection drawing of the arteriovenous communications in the anal submucosa; arteries white, veins stippled.

anorectal junction), the middle rectal artery pierced the rectal wall anterolaterally 3–4 cm above the levatores ani—where the superior rectal artery normally traverses the muscle wall. It then ran down into the anal submucosa to supply whole segments of it in place of the superior rectal; in the case of the specimen referred to in parentheses above the entire anal submucosa was supplied by the two middle rectal arteries.

In summary the anal lining derives a rich blood supply from the superior, middle and inferior rectal arteries, whose branches reach the anal submucosa in a most varied way.

The venous system—venous dilatations: Each of the 50 adult specimens exhibited discrete dilatations on the course of the veins of the anal submucosal venous plexus. A typical X-ray is illustrated in *Fig.* 4 and the typical appearance of a latex-injected specimen is shown in *Fig.* 5. The dilatations may be fusiform, saccular or serpiginous and are confined to the lower half of the anal canal. Above the pectinate line they occur in greatest profusion and complexity, but a second series—fewer in number and with a tendency to be larger in size—occurs below it. In 3 specimens thrombosis (confirmed histologically) had occurred recently in a dilatation below the pectinate line; the appearance was the same as that known as 'perianal haematoma'.

Of the 10 infant specimens, venous dilatations were found in 8 (*Fig.* 6). The 2 specimens in which they were absent were obtained from the bodies of very small stillbirths.

The venous system—portosystemic communications: Free communications both below and through the anal sphincter were demonstrated between the tributaries of the superior, middle and inferior rectal veins in all 25 specimens in which dissection was possible (the ones in which the veins had been injected with latex). They were also seen in all 25 specimens where radiography was employed (*see Fig.* 4), although the two-dimensional limitations of the X-rays precluded determination of their exact course. The communicating veins passing below the anal sphincter to join the subcutaneous tributaries of the inferior rectal vein were seen in all the specimens in which the anal canal lining had been removed and rendered translucent (*see Figs.* 5, 6).

Arteriovenous communications: In the specimen prepared for their demonstration red latex from the arterial side was seen under the dissecting microscope to have filled some of the venous dilatations by way of tiny direct arteriovenous communications. Because they wound through different planes it was not possible to demonstrate them photographically. A few dissected ones were sketched using the drawing attachment on a Wild Stereo-Zoom dissecting microscope; a drawing is illustrated in *Fig.* 7.

Treitz's muscle: Easily found in all 35 specimens, Treitz's muscle was seen to emerge from the internal sphincter at different levels in almost discrete, overlapping bands (*Fig.* 8). The bands passed downwards into the anal submucosa to form a continuous sheet on the deep surface of the submucosa from the pectinate line downwards. Microscopy demonstrated it to arise partly from the internal sphincter itself—the circular fibres of which seemed to curve inwards and downwards to form it—and partly from the conjoined longitudinal muscle, the contributing fibres passing between the imbricated fasciculi of the internal sphincter.

It was found to be distributed in three ways: to form a network around the haemorrhoidal venous plexus, to fan out into the perianal skin and to rejoin the longitudinal muscle (either around the lower border of the internal sphincter or through its lowermost fasciculus). It was found to contain a considerable amount of elastic tissue and to be hypertrophied, sometimes markedly so, in specimens exhibiting prolapsing haemorrhoids.

The anal 'cushions': As a result of the proctoscopic examination of patients with neither the symptoms nor signs of piles, the anal lumen was observed to form a more or less triradiate slit (*Fig*. 9). The stem of the 'Y' so formed was found invariably to approach the midline posteriorly, with its arms embracing a pad of tissue anteriorly or, more usually, in the right anterior position. The three folds thus separated three pads of tissue, the anal 'cushions', lying in the left lateral, right anterior and right posterior positions. Secondary folds were found to intersect the cushions to a variable degree. The anatomical dissections (*Fig*. 10) demonstrated the cushions to be caused by thickenings in the submucosa, and histology showed them to be composed largely of blood vessels (the venous dilatations making the main contribution), smooth muscle (Treitz's muscle) and elastic and connective tissue.

The columns of Morgagni are produced by longitudinal clefts in the anal cushions. With little doubt they represent the mechanism whereby the cushions are able to adapt to the large changes in size of the anal lumen. Their relationship to the anal cushions can only be seen properly in specimens in which the haemorrhoidal venous plexus has been filled.

The clinical study

Order of appearance of symptoms: The results from questioning 66 patients with prolapsing piles are displayed in *Fig*. 11. The majority of patients (60 per cent) claimed that prolapse had been the first symptom. Only 8 patients (12 per cent) thought that bleeding had started first, of whom one had a coexistent rectal polyp, one had anal fissure and a third gave an unreliable history, being mentally retarded. In only 5 patients, therefore, did it seem certain that the first manifestation of piles had been bleeding.

Histology of haemorrhoidectomy specimens: Twenty-five haemorrhoidectomy specimens were examined. They showed a stroma of connective tissue containing many blood vessels, and interweaving bundles of smooth muscle. Large vascular spaces were found to a greater or lesser extent in all the specimens, but apart from exhibiting evidence of recent or past thrombosis they were similar to the ones seen in the anal submucosa of cadaveric specimens in which there was no evidence of piles. There was no sign of vascular hyperplasia.

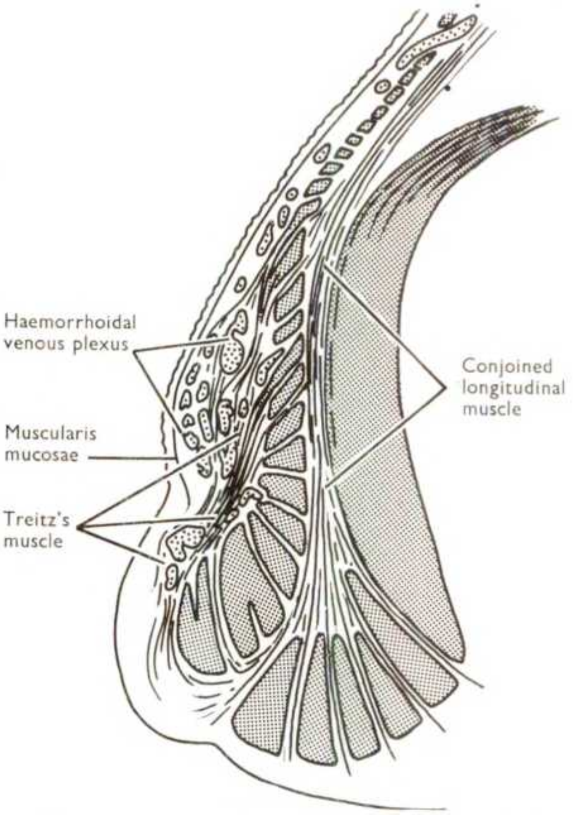


Fig. 8. A composite diagram of Treitz's muscle derived from longitudinal sections of the anal canal.

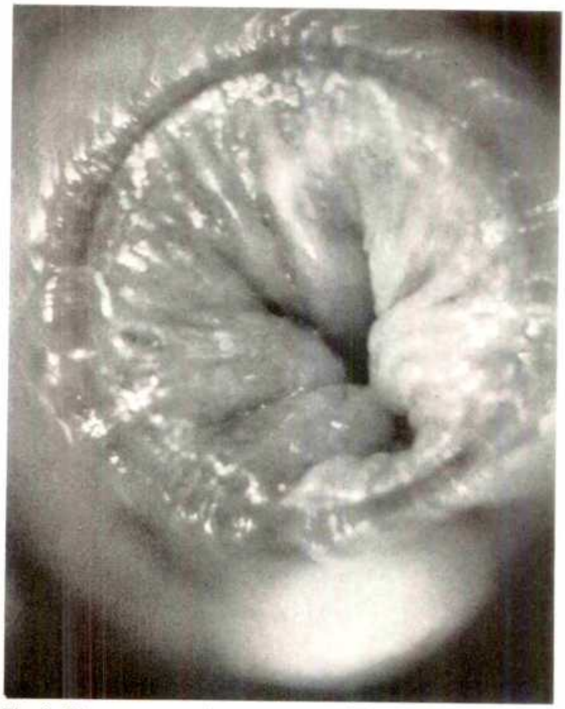


Fig. 9. The proctoscopic appearance of the anal 'cushions' in a normal individual. The triradiate configuration of the anal lumen is well shown.

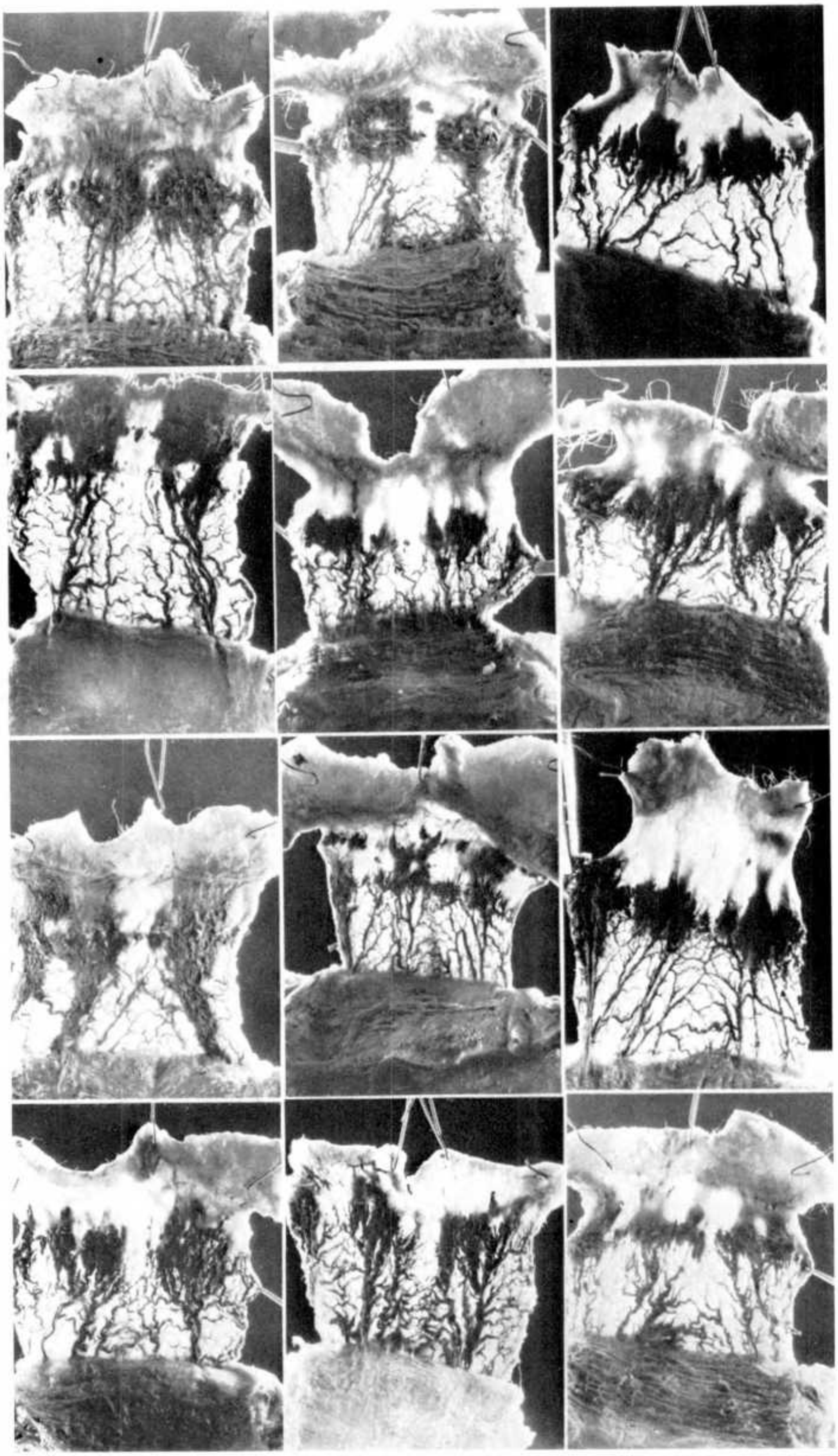


Fig. 10. Twelve anorectal specimens in which the anal lining has been dissected up and viewed with transmitted light. The arrangement of the anal cushions is similar.

The large vascular spaces were found to be deep in the substance of the pile, separated from the surface not only by connective tissue but by the muscularis mucosae. Many piles were noticed to have a red granular mucosa which histology revealed to be due to a rich network of dilated capillaries in the lamina propria (between the mucosal epithelium and the muscularis mucosae). Bleeding from these capillaries was clearly seen in some sections.

Discussion

The arterial system

Konstantinovitch (1872), Quénu (1893) and Widmer (1955) made dissections of the superior rectal artery; no other reports of personal dissections have been found in the literature. The present author's findings concerning its course and distribution are similar to theirs. None of them reported an arrangement similar to that described by Miles (1919), and Miles does not disclose the source of his information. No evidence from the author's dissections or from those reported by others supports his contention that the branching pattern of the superior rectal artery is responsible for the position of piles around the anal circumference.

The venous system

The present study has confirmed the observations of Sappey (1874), Duret (1877) and Waldeyer (1899) that the dilatations of the veins of the haemorrhoidal venous plexus are constant and normal structures, being present from birth and being found in all adults. Quénu (1892) seems to be the only one to have looked for them in children in vain. His failure was undoubtedly due to his technique—he was unable to cannulate the superior rectal vein in children because of its smallness and therefore could not inject it.

The findings of Cruveilhier (1867), Konstantinovitch (1872), Quénu (1892) and Tuttle (1906) concerning the abundance of communications between the portal and systemic circulations both below and through the anal sphincter have also been confirmed. The fact that Verneuil (1855a) was unable to find any at all and that Duret (1877) only found the ones passing through the sphincter is presumably attributable to technique.

Arteriovenous communications

Direct arteriovenous communications in the anal submucosa have been demonstrated by serial section (Stelzner et al., 1962) and by radiography (Schmidt and Staubesand, 1972) and now using the latex-injected preparation described here. As suggested by Staubesand et al. (1963), the anal submucosa may have an erectile property and the arteriovenous communications may function in the erectile mechanism. The enormous blood supply that the anal submucosa receives—greatly in excess of the conceivable metabolic requirements of its constituent cells—is further evidence for the existence of such a mechanism.

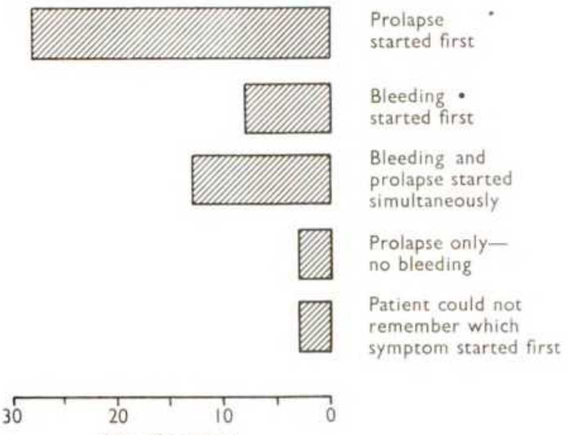


Fig. 11. The chronological order of appearance of symptoms in 66 patients admitted for treatment of prolapsing piles.

Treitz's muscle

As described by Treitz (1853), the haemorrhoidal venous plexus was found to be supported by a scaffold of smooth muscle and elastic tissue which was found to arise partly from the internal sphincter and partly from the conjoined longitudinal muscle. Both Treitz (1853) and Kohlrausch (1854) thought its function to be the support of the anal lining during defaecation. In view of the bulkiness of the anal lining (due to the anal cushions) and the strategic arrangement of the muscle their opinion is probably correct.

The anal cushions

Bourgery (1839) observed the anal lining to form a bolster, and Treitz (1853) also commented on its thickness. Stieve (1928) noted that it shared this characteristic with the mucosal lining of various other orifices in the body and suggested that its function was to assist in anal closure. As Staubesand et al. (1963) pointed out, an erectile mechanism would greatly enhance such a property.

The present study has shown that the submucosa does not form a continuous ring of thickened tissue in the anal canal but a discontinuous series of cushions, the three main ones being found constantly in the left lateral, right anterior and right posterior positions. Treitz (1853) also referred to cushions of tissue in the anal lining and noted that the submucosal smooth muscle contributes a great deal to their bulk. In the present study the haemorrhoidal venous plexus was found to be congregated within the cushions as well, not forming a uniform network around the anal canal. The dilatations of the veins obviously enable the cushions to vary considerably in size.

The segregation of the submucosal pad into separate cushions seems an ideal arrangement for adapting the anal canal lining to great changes in size of the lumen. The importance of the cushions may be judged from the fact that they are formed early on in embryonic life, as the illustrations in Johnson's (1914) paper on the development of the anorectum testify.

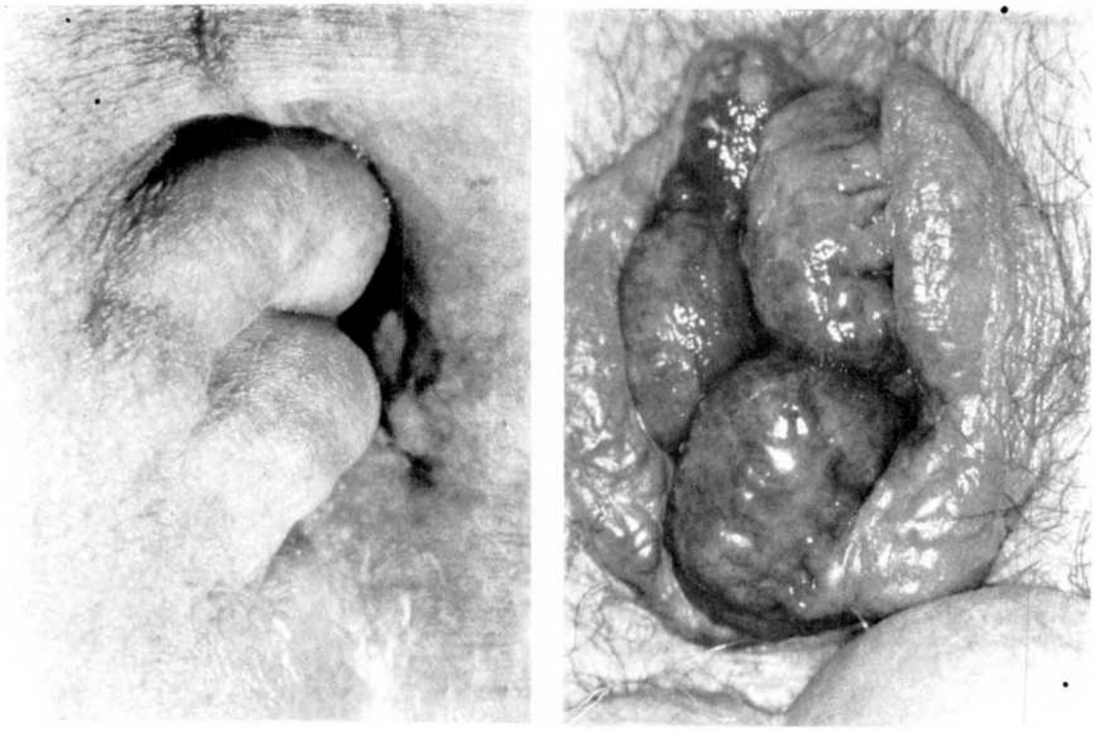


Fig. 12. *a*, Anal varices in a patient with portal hypertension due to cirrhosis of the liver. *b*, Prolapsed piles.

What are haemorrhoids?

The varicose vein theory: Stemming from the assumption that the dilatations of the veins of the internal rectal venous plexus are the result of a pathological change, the varicose vein theory is shown to be invalid by the confirmation that the dilatations are in fact normal. Furthermore, there is no evidence of a restriction of venous drainage from the anus or of a high venous pressure developing there. The fact that piles are no more common in patients with portal hypertension than in the population at large (Hunt, 1958) is additional evidence against the theory, as is the fact that when anal varices occur as the result of portal hypertension (a rare event) the appearance is quite different from that of haemorrhoids (*Fig.* 12). The varicose vein theory also fails to account for the fact that piles are frequently single and more common in the right anterior position than elsewhere (Goodsall and Miles, 1900).

The vascular hyperplasia theory: The present histological studies, like those of Graham-Stewart (1962), suggest that haemorrhoidal bleeding comes not from the venous spaces ('arterialized' by direct communications or not) but from dilated capillaries in the lamina propria. Furthermore, although dramatic descriptions of haemorrhage are often given, only 1 patient in the present study was anaemic at the time of admission, and Graham-Stewart found only 1 patient to be anaemic in his series of 150 haemorrhoid sufferers.

Although it is generally taught that bleeding is the first manifestation of piles (Gabriel, 1963; Goligher, 1967), there appears to have been no study, apart from the present one, which has been aimed at examining this dictum. The present findings suggest that bleeding is usually the later symptom and probably secondary to prolapse.

There is, therefore, neither histological nor circumstantial evidence to support the vascular hyperplasia theory.

The sliding anal lining theory: The discovery of the anal canal to be lined by specialized highly vascular cushions of submucosal tissue provides substantial support for the sliding anal lining theory. It would account for the regular appearance of piles in the right anterior, right posterior and left lateral positions and for their naked eye and histological appearances. Accepting that the cushions contribute to the mechanism of anal closure, it accounts for the high percentage of people who experience an impairment of continence after haemorrhoidectomy (Bennett et al., 1963). The triradiate configuration of the anal lumen due to the cushions might also explain the conflicting measurements of anal force as differently estimated by means of a force gauge and a balloon (Collins et al., 1967). That piles have been found to be associated with straining and an irregular bowel habit (Hyams and Philpott, 1970) is also compatible with the sliding anal lining theory. An irregular bowel habit is likely to be associated with hard and bulky stools, causing straining, which would be more likely to push the cushions out of the anal canal. Furthermore, straining, by producing a general increase in venous pressure, may cause engorgement of the cushions during defaecation, making their displacement more likely. Treitz's muscle might become stretched and disrupted if repeatedly subjected to such forces, intermittent and then permanent prolapse of the cushions resulting. Perhaps the right anterior cushion is subjected to a greater downward force during defaecation than the others, accounting for its more frequent prolapse.

Anal compliance may also be a factor in the production of haemorrhoids and may be associated with diet and stool consistency, accounting for the geographical distribution of the condition (Burkitt, 1972). If the anal canal is narrow and relatively rigid the cushions would be more likely to be pushed out on defaecation (perhaps helping to explain the success reported for forcible anal dilatation (Sames, 1972) in the treatment of piles).

Once prolapsed, the venous drainage from a haemorrhoid may be impeded by anal closure on the superior and middle rectal tributaries and by kinking of the inferior ones. The pile (displaced anal 'cushion') would then become engorged and therefore more difficult to replace. Such a situation may predispose to thrombosis—an 'attack of the piles'.

The success accorded to injection (Goligher, 1967) and banding (Barron, 1963) in the treatment of prolapsing piles is probably attributable to fibrosis in the cushion and a reduction in its size respectively.

In summary, the available evidence suggests that the theory that piles are nothing more than a sliding downwards of part of the anal canal lining is probably the correct one.

Acknowledgements

I would like to thank Mr T. Rowntree, Mr J. D. Jenkins, Dr J. Guthrie and the staff of the Morbid Anatomy Department, Southampton, Professor Sir James Fraser and the Wessex Regional Health Authority; without their help and encouragement this work could never have been undertaken.

References

ALLINGHAM W. (1873) *Diseases of the Rectum*, 2nd ed. London, Churchill, p. 73.

ALLINGHAM W. and ALLINGHAM H. W. (1896) *The Diagnosis and Treatment of the Diseases of the Rectum*, 6th ed. London, Baillière Tindall & Cox, pp. 108–115.

BARRON J. (1963) Office ligation for internal haemorrhoids. *Am. J. Surg.* **105**, 563–570.

BENNETT R. C., FREIDMAN M. H. W. and GOLIGHER J. C. (1963) Late results of haemorrhoidectomy by ligature and excision. *Br. Med. J.* **2**, 216–219.

BÉRAUD M. (1858) Du mode de terminaison des fibres longitudinales du rectum. *Gaz. Méd. Paris*, pp. 201–202.

BOURGERY J. M. (1839) *Traité Complet de l'Anatomie de l'Homme, comprenant la Médecine Opératoire*, Vol. 5. Paris, C. A. Delauney, p. 182.

BOURGERY J. M. (1840) *Traité Complet de l'Anatomie de l'Homme, comprenant la Médecine Opératoire*, Vol. 7. Paris, C. A. Delauney, p. 161.

BURKITT D. P. (1972) Varicose veins, D.V.T. and haemorrhoids; epidemiology and suggested aetiology. *Br. Med. J.* **2**, 556–561.

COLLINS C. D., DUTHIE H. L., SHELLEY T. and WHITTAKER G. E. (1967) Force in the anal canal and anal continence. *Gut* **8**, 354–360.

CRUVEILHIER J. (1852) *Traité d'Anatomie Pathologique*, 2nd ed. Paris, J. B. Baillière, pp. 816–817.

CRUVEILHIER J. (1867) *Traité d'Anatomie Descriptive*, 4th ed, Vol. 3, Part 1. Paris, P. Asselin, pp. 238–243.

CULLING C. F. A. (1963) *Handbook of Histological Techniques*, 2nd ed. London, Butterworths, pp. 437–438.

DURET H. (1877) Note sur la disposition des veines du rectum et de l'anus, et sur quelques anastomoses peu connues du système porte. *Bull. Soc. Anat. Paris* **52**, 168–176.

ELLIS G. V. and FORD G. H. (1867) *Illustrations of Dissections*. London, James Walton, p. 243.

FINE J. and LAWES C. H. W. (1940) On the muscle-fibres of the anal submucosa with special reference to the pecten band. *Br. J. Surg.* **27**, 723–727.

FORGUE E. and MILHAUD (1923) La circulation du segment sigmoido-rectal. *Rev. Chir.* **61**, 61–87.

GABRIEL W. B. (1963) *The Principles and Practice of Rectal Surgery*, 5th ed. London, Lewis, pp. 110–114.

GASS O. C. and ADAMS J. (1950) Haemorrhoids: aetiology and pathology. *Am. J. Surg.* **79**, 40–43.

GOLIGHER J. C. (1967) *Surgery of the Anus, Rectum and Colon*, 2nd ed. London, Baillière, Tindall & Cassell, pp. 111–115.

GOODSALL D. H. and MILES W. E. (1900) *Diseases of the Anus and Rectum*, Part I. London, Longmans Green, pp. 23, 29–34, 251–311.

GRAHAM-STEWART C. W. (1962) Injection treatment of haemorrhoids. *Br. Med. J.* **1**, 213–216.

GRAHAM-STEWART C. W. (1963) What causes haemorrhoids? *Dis. Colon Rectum* **6**, 333–344.

HUGHES E. S. R. (1957) *Surgery of the Anus, Anal Canal and Rectum*. Edinburgh, Livingstone, pp. 2, 129–131.

HUNT A. H. (1958) *A Contribution to the Study of Portal Hypertension*. Edinburgh, Livingstone, p. 61.

HUNTER J. (1728–1793) Hunterian Manuscripts (W. Clift's transcript), *Cases in Surgery*, Vol. ii, pp. 95–96.

HUNTERIAN MUSEUM (1848) *Descriptive Catalogue of the Pathological Specimens in the Hunterian Museum, Royal College of Surgeons of England*, Vol. III, Specimen 1277. London, William Clowes.

HYAMS L. and PHILPOTT J. (1970) An epidemiological investigation of haemorrhoids. *Am. J. Proctol.* **21**, 177–193.

JACKSON C. C. and ROBERTSON E. (1965) Etiologic aspects of haemorrhoidal disease. *Dis. Colon Rectum* **8**, 185–189.

JOHNSON F. P. (1914) The development of the rectum in the human embryo. *Am. J. Anat.* **16**, 1–53.

KOHLRAUSCH O. (1854) *Zur Anatomie und Physiologie der Beckenorgane.* Leipzig, S. Hirzel, pp. 9–10.

KONSTANTINOVITCH (1872) *Petersburg Med. Z.* **3**, 529, quoted by FORGUE and MILHAUD (1923), WIDMER (1955) and POIRIER and CHARPY (1895).

MALGAIGNE J. F. (1837) *Manual de Médecine Opératoire*, 10th ed. Paris, Germer Baillière, p. 581.

MILES W. E. (1919) Observations upon internal piles. *Surg. Gynecol. Obstet.* **29**, 497–506.

MORGAGNI J. B. (1749) *Seats and Causes of Diseases*, Vol. 2, Letter 32, Article 10. Translated by Benjamin Alexander, 1769. London, A. Millar, pp. 105–106.

PARKS A. G. (1955) De Haemorrhois. *Guys Hosp. Rep.* **104**, 135–156.

PARKS A. G. (1956) The surgical treatment of haemorrhoids. *Br. J. Surg.* **43**, 337–351.

PATEY D. (1972) Aetiology of varicosity (letter to the Editor). *Br. Med. J.* **2**, 712.

PENNINGTON J. R. (1923) *A Treatise on the Diseases and Injuries of the Rectum, Anus and Pelvic Colon.* Philadelphia, P. Blakiston, pp. 408–435.

PHILLIPS S. F. and EDWARDS D. A. W. (1965) Some aspects of anal continence. *Gut* **6**, 395–406.

POIRIER P. and CHARPY A. (1895) *Traité d'Anatomie Humaine.* Vol. 4, Part I. Paris, Masson et Cie, p. 365.

QUÉNU E. (1892) Étude sur les veines du rectum et de l'anus. *Soc. Anat.* pp. 601–609.

QUÉNU E. (1893) Des artères du rectum et de l'anus chez l'homme et chez la femme. *Bull. Soc. Anat.* **7**, 703–708.

QUÉNU E. and HARTMANN H. (1895) *Chirurgie du Rectum.* Paris, G. Steinheil, pp. 335–373.

ROUX C. (1881) Beiträge zur Kenntniss der Aftermuskulatur des Menschen. *Arch. Mikr. Anat.* **19**, 721–733.

SAMES P. (1972) Experiences of Lord's procedure for the treatment of haemorrhoids. *Proc. R. Soc. Med.* **65**, 782–783.

SAPPEY PH. C. (1874) *Traité d'Anatomie Descriptive*, 2nd ed, Vol. 4. Paris, Adrian Delahaye, p. 276.

SCHMIDT H. and STAUBESAND J. (1972) Der röntgenologische Nachweis des corpus cavernosum recti. *Fortschr. Röntgenstr.* **116**, 297–305.

STAUBESAND J., STELZNER F. and MACHLEIDT H. (1963) Über die "Goldenen Adern"—ein Beitrag zur Histophysiologie der sogenannten Glomerula venosa haemorrhoidalia. *Morph. Jb.* **104**, 405–419.

STELZNER F., STAUBESAND J. and MACHLEIDT H. (1962) Das Corpus cavernosum recti—die Grundlage der inneren Hämmorrhoiden. *Langenbecks Arch. Klin. Chir.* **299**, 302–312.

STELZNER F. (1963) Die Hämorrhoiden und andere Krankheiten des Corpus cavernosum recti und des Analkanals. *Dtsch. Med. Wochenschr.* **88**, 689–696.

STIEVE H. (1928) Ueber die Bedeutung venöser Wundernetze für den Verschluss einzelner Oeffnungen des menschlichen Korpers. *Dtsch. Med. Wochenschr.* **3**, 87–90.

TOMPSETT D. H. (1970) *Anatomical Techniques*, 2nd ed. Edinburgh, Livingstone, pp. 24–25.

TREITZ (1853) Ueber einen neuen Muskel am Duodenum des Menschen, über elastische Sehnen, und einige andere anatomische Verhältnisse. *Viertel Jahrschrift Prar. Heilkunde (Prager)* **1**, 113–144.

TUTTLE J. P. (1906) *A Treatise on Diseases of the Anus, Rectum and Pelvic Colon*, 2nd ed. New York, Appleton, p. 30.

VELPEAU A. L. M. (1826) *Traité d'Anatomie Chirurgicale*, Vol. 2. Paris, Crevot, pp. 320–324.

VERNEUIL M. (1855a) L'anatomie des hémorrhoides. *Bull. Soc. Anat.* **30**, 175–177.

VERNEUIL M. (1855b) L'anatomie pathologique des hémorrhoides. *Bull. Soc. Anat.* **30**, 191–192.

VIRCHOW R. (1863) Die krankhaften Geschwulste. Berlin. Quoted by PENNINGTON (1932).

WALDEYER W. (1899) Das Becken, mit besonderer Berücksichtigung der Chirurgie und Gynaecologie. Bonn, Freidrich Cohen. Quoted by STAUBESAND et al. (1963).

WARWICK R. and WILLIAMS P. L. (1973) *Gray's Anatomy*, 35th ed. Edinburgh, Longmans, p. 665.

WIDMER O. (1955) Die Rectalarterien des Menschen. *Z. Anat. Entwicklungsgesch.* **118**, 398–416.

DISPRAY I
Trade Mark
Quick Prep
Chlorhexidine gluconate 0.5% w/v in 70% I.M.S.
Stuart Pharmaceuticals Limited Cheadle, Cheshire.
DISPRAY 2
Hard Surface Disinfectant
Chlorhexidine gluconate 0.02% w/v in 70% I.M.S.

DISPRAY I

TRADE MARK

Quick Prep

Chlorhexidine Gluconate 0.5% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for skin disinfection

'Dispray' 1 Quick Prep.
(formerly known as Hibispray 1)
is an ideal preparation for skin and
hand disinfection in the busy
hospital environment.
At the touch of a button it gives
fast, easy and economical
skin disinfection prior to surgery,
injection or venepuncture.
When colour delineation
is required eg. pre-operatively,
'Dispray' 3 is available
with a red dye.

The 'Dispray' range
combines effectiveness with
convenience and economy.

Instant Availability.
No solutions to prepare.

Easy to use.
No swabs or bottles required.

Quick and Effective.
Rapid bactericidal action.

Efficient Application.
No wasted solutions.

Contents cannot
be contaminated.
No rejected solutions.

Long Lasting.
Contents of one can treat 100 sq. ft.

'Dispray' 1, 2, 3.
The Pick of the Bunch
for Disinfection.

DISPRAY 2

TRADE MARK

Hard Surface Disinfectant

Chlorhexidine Gluconate 0.02% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for hard surface disinfection

'Dispray' 2 Hard Surface
Disinfectant (formerly known as
Hibispray 2) provides rapid
disinfection of all hard surfaces
throughout the hospital.
Trolleys, cabinets, cupboards,
working surfaces – even footwear,
are rapidly, effectively
and efficiently disinfected.

Further
information
is available
from:

STUART

Stuart
Pharmaceuticals
Limited,
Carr House,
Carrs Road,
Cheadle,
Cheshire SK8 2EG.

for Foley read Argyle

Read why the Argyle Foley Catheter is simpler, safer, surer than any other Foley catheter

Symmetrical rounded tip and perfectly smooth finish for greater patient comfort.

Eyes specially shaped and positioned to maximise flow and minimise risk of occlusion.

Reinforced retention balloon. Doubly tested to inflate symmetrically and to deflate to a flat surface for smooth withdrawal.

Occlusion-free, integrally constructed funnels.

The Univalve system provides leak-free inflation control.

Highest quality latex provides strong yet flexible wall with a smooth circular lumen for efficient drainage.

Silicone-treated latex for inertness.

Sizes from 12Ch to 30Ch, all colour coded.

Argyle

Foley Catheter

Sherwood
MEDICAL INDUSTRIES

Sherwood Medical Industries Limited,
London Road, County Oak, Crawley, West Sussex, RH10 2TL.
Telephone: Crawley (0293) 34501. Telegrams: Shermed Crawley. Telex: 87685.

CAT Nos 5ml Balloon MAR 4405, 30ml Balloon MAR 4430

'Argyle' is a trade mark.

0044

Br. J. Surg. Vol. 62 (1975) 553–555

Localization of parathyroid adenomas by computer-assisted parathyroid scanning

P. J. ELL, A. TODD-POKROPEK AND K. E. BRITTON*

SUMMARY

In an attempt to localize adenomas of the parathyroid glands 36 patients with suspected hyperparathyroidism were studied with a computer-assisted double isotope scanning technique. Six patients were excluded from the statistical analysis because of uninterpretable scans. A definite localization was made with the computer-assisted scan in 16 patients. In 14 of these patients the site of the tumours was correctly predicted. In 14 patients no localization was seen on the scan. Four of these patients were classified as false negatives.

In 14 out of the 16 correctly localized tumours two-thirds had weights equal to or less than 1·5 g.

A NON-INVASIVE technique is required for localizing parathyroid adenomas before surgery since generally no diagnosis can be made on clinical grounds as to the side and site of the lesion. The most accurate method currently available for the localization of parathyroid adenomas is by radio-immunoassay of parathyroid hormone in samples obtained by direct venous catheterization (O'Riordan et al., 1971; Powell et al., 1972; Auerbach et al., 1973; Eisenberg et al., 1974). Although a considerable improvement over the previous techniques, it still suffers from being an invasive method, a lengthy procedure in time and requiring the administration of an average of 100 g of iodide to the patient.

Traditional scanning procedures using ^{75}Se selenomethionine have proved to be unsatisfactory in localizing functioning adenomas of the parathyroid glands (Garrow and Smith, 1968; Di Giulio and Beierwaltes, 1968; McGeown et al., 1968), particularly if these are below 2 g in weight. Diffuse hyperplastic glands also escape visualization (Di Giulio and Morales, 1969; Keeling and Todd-Pokropek, 1969). Part of the difficulty with these procedures may lie in the fact that the thyroid also takes up ^{75}Se selenomethionine. To overcome this problem a technique of subtracting a ^{125}I iodide thyroid scan from the ^{75}Se selenomethionine thyroid plus parathyroid scan has been devised.

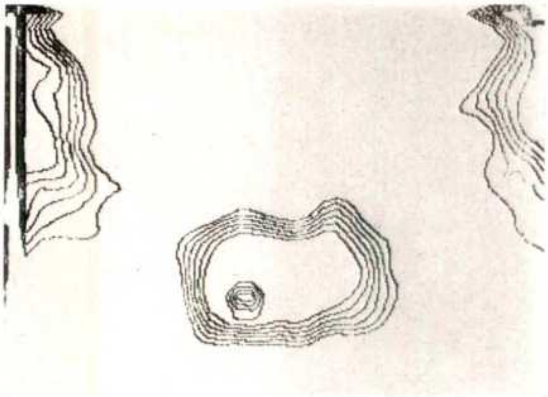


Fig. 1. A right inferior lesion is evident within the thyroid contour.

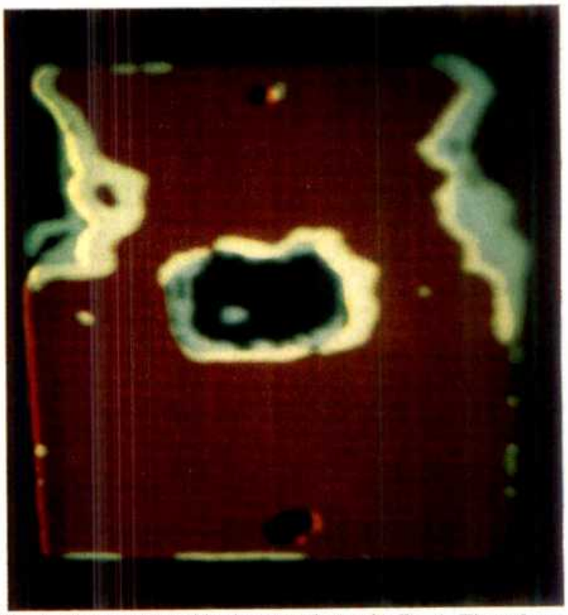


Fig. 2. The parathyroid adenoma shown in *Fig.* 1. The colour bands represent different levels of count rate.

Methods

Each patient receives 100 μCi ^{125}I sodium iodide orally 24 hours before and 250 μCi ^{75}Se selenomethionine intravenously 15 minutes before scanning the neck using the upper detector of a Selo DS4/45 double-headed scanner. The scan takes 20 minutes. The data on the distribution of each isotope are recorded separately at 3-mm intervals and registered by a two-channel punched paper tape system. The paper tape is then read into the departmental Varian 620i computer system. The data are manipulated by a scan analysis program. Two matrices are created for the two radionuclide distributions. Each point in a matrix corresponds to a point in the scan of the neck. The value at a point in the matrix represents the count density at that point in the scan. The 'peak

---

* Department of Nuclear Medicine, The Middlesex Hospital Medical School, London.

Table I: SUMMARY OF RESULTS

Case no.	Scan		Operation findings	Final diagnosis
	Original	Computer		
1	−	+	1·6-g right anterior mediastinum adenoma	Parathyroid adenoma
2	−	+	1·3-g right inferior adenoma	Parathyroid adenoma
3	−	±	250-mg right inferior adenoma	Parathyroid adenoma
4	+	+	1-g left superior adenoma	Parathyroid adenoma
5	−	−	No operation yet	Probable parathyroid adenoma
6	−	−	No operation yet	Probable parathyroid adenoma
7	−	−	No operation yet	Probable parathyroid adenoma
8	−	−	No operation yet	Probable parathyroid adenoma
9	−	−	Operation negative	Possible parathyroid adenoma
10	−	−	No operation yet	Milk alkali. Adenoma
11	+	+	3·5-g right inferior adenoma	Parathyroid adenoma
12	−	±	Hyperplasia	Recovery from raised calcium
13	−	−	2·5-g left inferior adenoma	Parathyroid adenoma
14	−	±	Hyperplasia	Probable parathyroid adenoma
15	−	−	No operation yet	Recovery from raised calcium
16	−	±	Operation negative	Recovery from raised calcium
17	−	−	Operation negative	Recovery from raised calcium
18	−	+	Not explored	? Primary aldosteronism
19	−	+	Operation negative	Recovery from raised calcium
20	−	±	Operation negative	Recovery from raised calcium
21	−	−	Hyperplasia	Probable parathyroid adenoma
22	±	±	1·5-g right inferior adenoma	Parathyroid adenoma
23	−	+	1·3-g right inferior adenoma	Parathyroid adenoma
24	+	+	1-g right inferior adenoma + 1·5-g left inferior adenoma	Parathyroid adenoma
25	+	+	1·4-g left inferior adenoma	Parathyroid adenoma
26	−	+	2·0-g right superior adenoma	Parathyroid adenoma
27	−	+	3·0-g right inferior adenoma	Parathyroid adenoma
28	−	+	1·1-g left superior adenoma	Parathyroid adenoma
29	−	−	0·2-g left superior adenoma	Parathyroid adenoma
30	−	−	No operation yet	Possible parathyroid adenoma
31	−	+	1·5-g left inferior adenoma	Parathyroid adenoma
32	−	−	No operation yet	Sarcoidosis
33	−	−	2·5-g left inferior adenoma	Parathyroid adenoma
34	−	+	1·5-g right superior adenoma	Parathyroid adenoma
35	−	+	1·3-g right superior adenoma	Parathyroid adenoma
36	−	+	1·0-g left inferior adenoma	Parathyroid adenoma

Key: − : Negative; + : Positive; ± : Equivocal.

count' of a matrix is chosen as that position at which the sum of the counts within a 3 × 3 element area is a maximum. A scaling factor is determined as the ratio of the 'peak count' in the iodide scan matrix and the equivalent point in the selenomethionine scan matrix. The thyroid scan matrix is then subtracted, element by element, from the scaled-up matrix of the thyroid plus parathyroid scan. To reduce the effect of count rate fluctuations, the resulting image undergoes a 9-point smoothing procedure. The image is then interpretable, but of low contrast. An interactive colour television display is used to determine the appropriate levels of background subtraction and contrast enhancement. The final hard copy output is either as a contour map provided by an electrostatic plotter (*Fig.* 1) or recently as an SX70 colour Polaroid print of the television display (*Fig.* 2).

Table II: SCAN REPORTS COMPARED WITH CLINICAL FOLLOW-UP AND SURGICAL EXPLORATION OF THE NECK

	Digital scan	Tumour present	Tumour not confirmed
Positive	16	14	2
Negative	14	3	11

$x^2 = 13·27$, $P < 0·001$.

Table III: SITE AND WEIGHT OF THE TUMOURS CORRECTLY DIAGNOSED ON THE SCAN

	Right			Left	
Superior	2	1·3		1·1	
	1·5			1·1	
Inferior	3·5	1·0		1·5	1·5
	1·3	1·3	3·0	1·4	1·0

Results

This study concerns a series of 36 patients with suspected hyperparathyroidism (*Table I*), none of whom had an abnormal palpable mass in the neck. Useful information was obtained from the routine unprocessed scan in only 4 cases. The results of computer-assisted scanning were compared with the data obtained from surgical exploration of the neck and clinical follow-up (*Table II*). Six patients with uninterpretable scans were excluded from the statistical analysis.

A definite localization was made with the computer-assisted parathyroid scan in 16 patients. In 14 of these the site of the tumour was correctly predicted. In the remaining 14 patients no evidence of focal increase of the ^{75}Se selenomethionine was seen on the scan. Of these, 4 were classified after operation and follow-up as false negatives. From 14 out of the 16 tumours which were correctly localized on the scan

10 had weights equal or below 1·5 g; the remaining tumours had weights between 1·6 and 3·5 g.

The false negatives included 1 case of diffuse hyperplasia and 3 cases of parathyroid adenoma. Two of these adenomas (*Cases* 13 and 33) were situated retrosternally and would be obscured as a result of uptake of selenomethionine by normal bone marrow, and the third was only 0·2 g in weight (*Case* 29). The anatomical sites of the correctly diagnosed tumours and the distribution of their weights are shown in *Table III*.

Two false positive scans were reported: 1 patient was not explored surgically and at follow-up no longer demonstrated hypercalcaemia; the other recovered from a persistently raised calcium level after a negative surgical exploration of the neck.

The 6 cases excluded from statistical analysis because of equivocal scans included 2 cases of hyperplasia (*Cases* 12 and 14), 2 cases with negative surgical exploration of the neck with recovery from raised serum calcium levels (*Cases* 16 and 20) and 2 cases of right inferior parathyroid adenoma (*Cases* 3 and 22), weighing 0·25 and 1·5 g respectively.

Discussion

The concept of subtracting an image of the thyroid from the composite thyroid plus parathyroid image is similar in principle to the usual method of pancreas scanning. The subtraction method highlights areas of increased selenomethionine concentration that are to be expected in parathyroid adenomas. The images are handled by an interactive computer system in order to make best possible use of the data.

The disadvantages of the technique are twofold: its dependence on the correct working of a sophisticated computer system and the problem of selenomethionine uptake by bone marrow. A midline concentration of activity due to the seventh cervical vertebra is usual and the retrosternal region is not accessible. A subtraction technique utilizing a bone-marrow-seeking agent, such as ^{111}In indium chloride, might circumvent this problem.

The advantages of the technique are its non-invasive nature, short investigation time and direct display on a two-dimensional map of the relation of the suspected adenoma to the thyroid gland. In this retrospective series approximately two-thirds of the correctly predicted tumours had weights equal to or less than 1·5 g.

Facilities for computer-assisted analysis of scan data are becoming generally available in regional centres for nuclear medicine. The place of computer-assisted parathyroid scanning is likely to be after a clear clinical and biochemical diagnosis of hyperparathyroidism has been made—a criterion not met in some patients in this pilot series due to lack of unequivocal biochemical confirmation of hyperparathyroidism. It appears that if definite localization is made by computer-assisted parathyroid scanning, then there may be less need for parathyroid venous sampling. An equivocal or negative result should not be relied upon. At present a comparison with the venous sampling technique is being attempted. This presents difficulties because if the venous sampling technique is performed after the scan the samples are contaminated with ^{75}Se selenomethionine, and if the venous sampling is before the scan the high iodide contrast media prevent an adequate thyroid scan. Substitution of ^{99}Tc^{m} pertechnetate for ^{125}I iodide has been partly successful in obtaining adequate thyroid scans in this situation. However, since the vascularity of some parathyroid adenomas may cause apparent uptake of pertechnetate (Arkles, 1974), this form of thyroid subtraction technique appears less reliable. A prospective study of computer-assisted parathyroid scanning using the technique described here is in progress. We hope these results will encourage others to re-evaluate the place of an advanced method of parathyroid scanning in locating preoperatively parathyroid adenomas.

Acknowledgements

We would like to thank Dr D. H. Keeling and Mr N. J. G. Brown for their help, Professor E. S. Williams for his interest and the consultants of many hospitals who referred patients for this study.

References

ARKLES L. B. (1974) Personal communication.

AUERBACH G. D., MALLETTE L. E., PATTEN B. N., HEATH D. A., DOPPMAN J. K. and BILEZIKIAN J. P. (1973) Hyperparathyroidism: recent studies. *Ann. Intern. Med.* **79**, 566–581.

EISENBERG H., PALLOTTA J. and SHERWOOD L. M. (1974) Selective arteriography, venography and venous hormone assay in diagnosis and localisation of parathyroid lesions. *Am. J. Med.* **56**, 810–820.

GARROW J. S. and SMITH R. (1968) The detection of parathyroid tumours by selenomethionine scanning. *Br. J. Radiol.* **41**, 307–311.

DI GIULIO W. and BEIERWALTES W. H. (1968) Parathyroid scanning. In: WANG Y. (ed.) *Advances in Dynamic Radio-isotope Scanning*. Springfield, Ill., Thomas.

DI GIULIO W. and MORALES J. O. (1969) The value of the selenomethionine Se75 scan in pre-operative localisation of parathyroid adenomas. *JAMA* **209**, 1873–1880.

KEELING D. H. and TODD-POKROPEK A. (1969) Computer assisted parathyroid scanning. In: *Medical Radioisotope Scintigraphy*, Vol. 1. Vienna, International Atomic Energy Agency, pp. 745–757. (I.A.E.A. STI/PUB/263.)

MCGEOWN M. A., BELL T. K., SOYAMMWO M. A. O., FENTON S. A. and OREOPOULOS D. (1968) Parathyroid scanning in the human with selenomethionine-75 Se. *Br. J. Radiol.* **41**, 300–306.

O'RIORDAN J. L. H., KENDALL B. E. and WOODHEAD J. S. (1971) Pre-operative localisation of parathyroid tumours. *Lancet* **2**, 1172–1175.

POWELL D., SHIMKIN P. M., DOPPMAN J. L., WELLS S., AURBACH G. D., MARX S. J., KETCHAM A. S. and POTTS J. T. (1972) Primary hyperparathyroidism, pre-operative tumor localization and differentiation between adenoma and hyperplasia. *New Engl. J. Med.* **286**, 1169–1175.

Br. J. Surg. Vol. 62 (1975) 556–559

True recurrence of hyperparathyroidism: proposed criteria of recurrence

H. MULLER*

SUMMARY

Although recurrent hyperparathyroidism should not be rare on theoretical grounds, only a few cases of proved recurrence have been reported in the literature. In the present author's series only 4 patients (1 per cent) had true recurrence. Criteria for recurrence were:

1. Histological identification by biopsy and frozen section of all the parathyroid glands at the first operation.

2. Complete removal of the enlarged gland(s).

3. A normocalcaemic period of at least 1 year.

4. The finding of a tumour at the site of a previously normal-sized gland.

The low incidence of recurrent hyperparathyroidism might be explained by the long period of time needed for the recurrence to develop. However, since diagnosis of hyperparathyroidism is now more easily made and patients are treated surgically earlier in the course of the disease, the incidence of true recurrence might be expected to rise. A meticulous exploration during operation and careful follow-up of the patients are therefore required.

IN the past three decades many articles have appeared on the diagnosis, pathophysiology and treatment of primary hyperparathyroidism. However, there are very few publications on the long term results of surgical treatment. It is difficult to obtain sufficient data on the percentage of patients with persistent or recurrent hypercalcaemia after a 'successful' operation, and very few articles give an indication of the incidence (Cope et al., 1961; Hellström, 1965; McGeown, 1965). Recent developments in pathophysiology and histology of parathyroid tumours make these data desirable. In earlier publications the incidence of hyperplasia of all the parathyroid glands or the occurrence of multiple tumours was reported to be low. However, after Cope et al. (1958) published an article on chief cell hyperplasia, others started to report the condition frequently. The present author's experience in over 400 patients confirms this and he is inclined to the view that hyperplasia is the main cause of hyperparathyroidism. Biopsies taken from enlarged and from normal-sized glands often show nodular hyperplasia, and this makes it impossible for the pathologist to conclude which of the biopsies is taken from the so-called 'adenoma'. This finding is in complete agreement with the opinion of Paloyan et al. (1973), who stated: 'The entire spectrum of adenoma, hyperplasia, transitional cells, and normal histology may present not only in a single patient, but in some instances in a single gland.' In view of this, it is not surprising that they found multiple gland involvement in 65 per cent of their patients. In many of the author's patients also one 'adenoma', two normal-sized glands and one slightly enlarged gland weighing 80–90 mg (twice the normal weight) were found, and yet histological examination of biopsies of all the glands showed nodular hyperplasia. Since many surgeons would remove only the evidently enlarged gland a recurrence of hyperparathyroidism could be expected in similar cases.

There are other reasons for suspecting that hyperparathyroidism may recur. It is well known that hyperparathyroidism occurs predominantly in postmenopausal women (Muller, 1969), a group of patients in whom osteoporosis and a slightly elevated serum calcium are frequent. This indicates that hyperparathyroidism could be a secondary reaction in these patients and that recurrence after removal of an enlarged gland could be expected theoretically. The role of vitamin D, and especially of 1,25-dihydrocholecalciferol in this aspect may be important. If parathormone is a trophic hormone for the production of 1,25-dihydrocholecalciferol (Rasmussen, 1972), there might well be some sort of feedback mechanism which could provide the stimulus for hyperparathyroidism.

Why are more and more cases with hyperplasia of all the parathyroid glands found early in the course of the disease? This is conspicuous if early publications, mostly of cases with long standing disease, are compared with recent investigations using screening methods (Hellström, 1965; Cope, 1966; Haff, 1971; Paloyan et al., 1973). Bruining (1971) suggested that an unknown stimulus causes hyperplasia of all the glands with outgrowth of one gland eventually suppressing the other glands, but this unknown stimulus could also cause recurrence years after removal of the 'primary' tumour. In some patients with familial hyperparathyroidism or multiple endocrine adenopathy, only one enlarged parathyroid is found, while other patients are found to have hyperplasia of all four glands. If the one enlarged gland is removed, it is conceivable that the primary stimulus remains, eventually causing recurrence.

In this context it seemed of interest to review the literature and a personal series of patients to determine the incidence of recurrent hyperparathyroidism. In order to do this, it is necessary to define 'recurrence' and 'persistent hypercalcaemia'. At operation a tumour can be left behind erroneously after removal of

---

* Department of Surgery, University Hospital Dijkzigt, Rotterdam Medical School, The Netherlands.

one or more 'adenomas'. The postoperative serum calcium levels will usually fall to normal or subnormal levels for some time, only to reach abnormally high levels again, often within a few weeks. If the patient is discharged from hospital in a relatively short time without adequate follow-up and is then readmitted because of recurrent clinical symptoms, a faulty diagnosis of recurrent, instead of persistent, hyperparathyroidism can be made. This happens only too often, especially when the surgeon is in the habit of terminating the operation when a large 'adenoma' is found, being afraid of damaging the other, presumably 'hypoplastic', parathyroids (Cope, 1966). In the author's experience the other parathyroids may be in a state of hypofunction, but are certainly not hypoplastic. The concept of 'recurrence' should be applied only to cases in which a previously normal-sized parathyroid has become a tumour. A true recurrence should therefore meet the following criteria:

1. All the glands are identified at the first operation and confirmed by biopsy and frozen section.
2. The enlarged glands are removed completely.
3. The patient has been normocalcaemic for at least a year since operation.
4. At reoperation a tumour is found at the site of a previously normal-sized gland.

Most reports fail to satisfy these strict criteria. In the excellent review of Norris (1947) of 322 cases no recurrences were mentioned, but at that time operative treatment of hyperparathyroidism had not been practised for long. Some of the published recurrences have been called carcinomas (Black and Ackerman, 1950; Kleinfeld, 1959; Ellis et al., 1971; Hill et al., 1972), but the differentiation of carcinoma from adenoma or even hyperplasia can be very difficult. Furthermore, the incidence of metastasizing carcinoma is very low. This makes it probable that many of the 'carcinomas' in reality are hyperplasias or adenomas. In the present series of over 400 cases no carcinoma was encountered, although the histology sometimes showed very 'wild' pictures with extensive areas of polymorphic cells. This confirms Dent's (1966) statement: 'The parathyroid gland appears to offer a unique opportunity for the study of tumour formation mechanisms, all stages from normal, through hyperplasia, to adenoma and finally cancer being readily available.' In some cases the recurrence stems from parts of the original benign tumour, intentionally or inadvertently left behind (Burk, 1947; Black and Ackerman, 1950; Keminger, 1964). It is regrettable that only a few authors describe the condition of the parathyroid glands not removed at operation (Greenfield et al., 1959; Haff et al., 1971; Clark and Taylor, 1972; Doury et al., 1973). Data about systematic biopsies with frozen section of all the glands are nearly always absent. In some papers on recurrent hyperparathyroidism (Shallow and Fry, 1948; Watanabe et al., 1961; Rienhoff et al., 1968; Fulmer et al., 1969; Cryer and Kissane, 1973) no search for the normal parathyroids was mentioned and no biopsies were taken for frozen section. Goldman et al. (1971) even warn against biopsy of normal glands since this might cause parathyroid infarction.

Perusal of the literature thus shows insufficient data on recurrent hyperparathyroidism and it seems very hazardous to advise subtotal parathyroidectomy as a routine procedure (Paloyan et al., 1969; Haff et al., 1971; Marsden and Day, 1973) solely on theoretical grounds. This might result in an unnecessarily high percentage of cases with persistent hypocalcaemia (Bruining, 1971). The present series of patients seemed well suited for a study of persistent and recurrent hyperparathyroidism, since the series is rather large and nearly all the patients were operated on by the same surgeon and the same routine was used throughout. Moreover an efficient follow-up in a small country like Holland is more feasible than in most other countries.

Observations

Of 394 patients, 62 were considered for further analysis, the other 332 patients having remained normocalcaemic since operation. Of these 62 patients, 46 were referred to the University Hospital Dijkzigt, Rotterdam, for reoperation after a negative exploration elsewhere or because of persistent hypercalcaemia in spite of removal of one or more tumours. An analysis of this group showed the following causes for hypercalcaemia: negative exploration(s) 44, other overlooked tumours 14 and true recurrences 4. Details of the 4 patients with time of recurrence are given below.

Case reports

Case 1: A woman, born in 1907, had had recurrent renal stones since 1945. In 1955 a diagnosis of hyperparathyroidism was made. At operation in June 1955 all four parathyroids were found and identified by biopsy and frozen section. The enlarged right lower parathyroid was removed (2·25 g). The other glands were normal. The patient was seen at regular intervals and in 1962 the serum calcium was still normal. Subsequently, the serum calcium rose to 11·5 mg/100 ml, and after clinical evaluation a further operation was performed (January 1964). Both upper parathyroids were enlarged and were therefore removed; each weighed approximately 200 mg. The remaining left lower parathyroid was normal. The patient has remained normocalcaemic.

Case 2: A woman, born in 1894, had had recurrent renal stones since 1953 with severe hypercalcaemia. A diagnosis of hyperparathyroidism was made and an operation followed (September 1955). The right upper, left upper and left lower glands were enlarged, the right lower one being normal. Biopsies of all the glands showed hyperplasia and the three enlarged glands were removed; they weighed 250, 500 and 600 mg respectively. Throughout 1964 the patient remained normocalcaemic. In 1967 hypercalcaemia was noted without any clinical manifestation of hyperparathyroidism. In view of her age she was treated with phosphate. She died in hospital in 1974 at the age of 80, and at autopsy a very large right lower parathyroid was found.

Case 3: A woman, born in 1916, had had recurrent renal stones since 1948. In 1956 severe hypercalcaemia was found and a diagnosis of hyperparathyroidism was made. At operation (October 1956) all four parathyroids were identified histologically by biopsy and frozen section. Only the enlarged left upper gland was removed (900 mg), the other three glands being of normal size. The serum calcium remained normal throughout 1964. From 1964 until 1972 serum calcium levels fluctuated between 10·7 and 11·7 mg/100 ml. A further operation was performed and a slightly enlarged left lower parathyroid was removed (September 1972). Since then she has remained normocalcaemic.

Case 4: A woman, born in 1924, had had recurrent attacks of cystopyelitis and general malaise since 1958. In 1960 rather severe hypercalcaemia was found and hyperparathyroidism was diagnosed. At operation (February 1960) all the parathyroids were identified by biopsy and frozen section and the enlarged right and left upper parathyroids were removed (800 and 200 mg respectively). Until 1966 the serum calcium levels remained normal, but they have risen slightly (11·0–11·5 mg/100 ml) since then. In 1970 a silent stone in the left kidney was found on X-ray, and re-exploration of the neck followed (February 1971). The left lower parathyroid was enlarged (250 mg) and removed. The right lower gland could not be found in the scar tissue. Presumably this gland was also hyperfunctioning since her serum calcium levels are still slightly elevated.

Discussion

As stated earlier there are several possible explanations for the development of true recurrence of hyperparathyroidism after adequate operative treatment, and it is surprising to find only a few definite cases in the literature. That true recurrence is very rare is confirmed by the extremely low figure of 1 per cent in the present series. However, this shows that recurrence does not usually develop for some years. In the 4 patients reported here the periods of proved normocalcaemia were 7, 9, 8 and 6 years respectively, and second operations were performed 9–16 years after the first explorations. It seems likely that more cases of true recurrence may be expected in the future since hyperparathyroidism is now diagnosed earlier in the course of the disease than it was formerly, and patients are followed up more carefully. Clearly, meticulous exploration of all four parathyroids, with biopsy and frozen section of all the glands, is needed at the first operation. Adherence to these rules will probably reduce greatly the number of cases with persistent hypercalcaemia. Follow-up at regular intervals seems necessary for many years after operation. Only in this way can an accurate assessment of the incidence of truly recurrent hyperparathyroidism be obtained.

References

BLACK B. K. and ACKERMAN L. V. (1950) Tumours of the parathyroid. A review of twenty-three cases. *Cancer* 3, 415–444.

BRUINING H. A. (1971) *Surgical Treatment of Hyperparathyroidism.* Assen, Van Gorcum.

BURK L. B. jun. (1947) Recurrent parathyroid adenoma. *Surgery* **21**, 95–101.

CLARK O. and TAYLOR S. (1972) Persistent and recurrent hyperparathyroidism. *Br. J. Surg.* **59**, 555–558.

COPE O. (1966) The story of hyperparathyroidism at the Massachusetts General Hospital. *New Engl. J. Med.* **274**, 1174–1182.

COPE O., BARNES B. A., CASTLEMAN B., MUELLER G. C. E. and ROTH S. I. (1961) Vicissitudes of parathyroid surgery: trials of diagnosis and management in 51 patients with a variety of disorders. *Ann. Surg.* **154**, 491–508.

COPE O., KEYNES W. M., ROTH S. I. and CASTLEMAN B. (1958) Primary chief-cell hyperplasia of the parathyroid glands: a new entity in the surgery of hyperparathyroidism. *Ann. Surg.* **148**, 375–389.

CRYER P. E. and KISSANE J. (1973) Hyperparathyroidism. *Am. J. Med.* **55**, 657–666.

DENT C. E. (1966) Parathyroid disease. *Ann. R. Coll. Surg. Engl.* **39**, 150.

DOURY P., CHIGOT P.-L., DULAC J.-F., LIÈVRE J.-A., RONDOT P., MASBERNARD A., PATTIN S. and GIUDICELLI C. (1973) Hyperparathyroïdisme récidivant et familial à début pseudo-myopathique et avec atteinte neurologique centrale. *Ann. Méd. Interne* (*Paris*) **124**, 617–623.

ELLIS H. A., FLOYD M. and HERBERT F. K. (1971) Recurrent hyperparathyroidism due to parathyroid carcinoma. *J. Clin. Pathol.* **24**, 596–604.

FULMER D. H., ROTHSCHILD E. O. and MYERS W. P. L. (1969) Recurrent parathyroid adenoma. *Arch. Intern. Med.* **124**, 495–501.

GOLDMAN L., GORDAN G. S. and ROOF B. S. (1971) The parathyroids. Progress, problems and practice. *Curr. Probl. Surg.* Aug, pp. 1–64.

GREENFIELD J. C. jun., VERNER J. V. jun. and ENGEL F. L. (1959) Hyperparathyroidism recurring ten years after removal of parathyroid adenoma. *JAMA* **171**, 164–167.

HAFF R. C. and BALLINGER W. F. (1971) Causes of recurrent hypercalcemia after parathyroidectomy for primary hyperparathyroidism. *Ann. Surg.* **173**, 884–891.

HELLSTRÖM J. (1965) The treatment of hyperparathyroidism. *Urol. Int.* **19**, 124–130.

HILL C. S. jun., OUAIS S. G. and LEISER A. E. (1972) Long-term administration of calcitonin for hypercalcemia secondary to recurrent parathyroid carcinoma. *Cancer* **29**, 1016–1020.

KEMINGER K. (1964) Hyperparathyroidismusrezidiv nach Autoimplantation. *Klin. Med.* **19**, 455–461.

KLEINFELD G. (1959) A clinical and pathological study of 63 functioning parathyroid tumors. *Cancer* **12**, 902–911.

MCGEOWN M. G. (1965) The results of parathyroidectomy. *Urol. Int.* **19**, 137–143.

MARSDEN PH. and DAY J. L. (1973) Hyperparathroidism: the risk of recurrence. *Clin. Endocrinol.* **2**, 9–13.

MULLER H. (1969) Sex, age, and hyperparathyroidism. *Lancet* **1**, 449–450.

NORRIS E. H. (1947) The parathyroid adenoma. A study of 322 cases. *Int. Abstr. Surg.* **84**, 1–41.

PALOYAN E., LAWRENCE A. M., BAKER W. H. and STRAUS F. H. (1969) Near-total parathyroidectomy. *Surg. Clin. North Am.* **49**, 43–48.

PALOYAN E., PALOYAN D. and PICKLEMAN J. R. (1973) Hyperparathyroidism today. *Surg. Clin. North Am.* **53**, 211–220.

RASMUSSEN H., WONG H. M., BICKLE D. and GOODMAN D. B. R. (1972) Hormonal control of the renal conversion 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol. *J. Clin. Invest.* **51**, 2502–2504.

RIENHOFF W. F. jun., RIENHOFF W. F. III, BRAWLEY R. K. and SHELLEY W. M. (1968) The surgical treatment of hyperparathyroidism. *Ann. Surg.* **168**, 1061–1074.

SELDIN D. W. (1970) Case records of the Massachusetts General Hospital. *New Engl. J. Med.* **282**, 1028–1037.

SHALLOW T. A. and FRY K. E. (1948) Parathyroid adenoma. Occurrence in father and daughter. *Surgery* **24**, 1020–1025.

WATANABE M., BAXTER S. and BECK J. C. (1961) Hyperparathyroidism due to late recurrence of parathyroid adenoma. Report of two cases. *Am. J. Med.* **31**, 498–504.

YOUNG M. M. and NORDIN B. E. C. (1967) Calcium metabolism and the menopause. *Proc. R. Soc. Med.* **60**, 1137–1138.

Br. J. Surg. Vol. 62 (1975) 560–562

Recurrent pleural effusion in chronic relapsing pancreatitis

RUDRA RASARETNAM, A. B. V. PERERA AND M. KUMARASINGHE*

SUMMARY

A case of recurrent pleural effusion occurring in a patient with chronic relapsing pancreatitis is presented. Although it is one of the less common manifestations of the pleuropulmonary complications of pancreatitis, the presence of such a lesion is of diagnostic importance when the enzyme content of the effusion is elevated above the levels in the serum. In most of the reported cases resolution has occurred with conservative therapy, but failure to do so necessitated subtotal pancreatectomy, following which the patient made an uneventful recovery.

ALTHOUGH many accounts make no mention of the pleuropulmonary complications of pancreatitis, retrospective analyses have shown a high incidence of raised hemidiaphragm, basal atelectasis, pleural reaction and pleural effusion (Lipp and Aaron, 1950; Hammarsten et al., 1959; Kaye, 1968). Most of these reactions are non-specific, occurring in many acute upper abdominal lesions, mainly subphrenic abscesses (Ochsner and DeBakey 1938). Pleural effusions are reported to occur in between 3 and 38 per cent of cases of pancreatitis and are predominantly on the left, and although relatively uncommon, they can be of diagnostic significance when shown to contain a high level of pancreatic enzymes.

Case report

S. E. F., a 45-year-old man, was admitted to a medical unit of the Colombo General Hospital in March 1972 with a history of gradual onset of epigastric pain of 9 days' duration, which was becoming progressively worse. After a barium meal examination of the upper gastro-intestinal tract, which showed no abnormality, he was discharged on the ninth day, but was readmitted the same night with severe abdominal pain. At operation he had free fluid in the peritioneal cavity, the omentum was oedematous and there were numerous patches of fat necrosis. The pancreas was firm. A diagnosis of acute pancreatitis was made, and his postoperative recovery was uneventful.

The patient had been accustomed to taking half a bottle of arrack daily for the past 20 years, and he continued to do so after his discharge from hospital. Over the next 2 years he complained of attacks of abdominal pain, which lasted only 5 minutes and occurred shortly after the start of a meal. There was no radiation of pain and no vomiting.

In March 1974 he developed more severe abdominal pain, and 3 days before admission he also noticed increasingly severe pain in the right lower chest. He also complained of pain in the right shoulder and retrosternal pain which radiated up into the neck, but was not associated with sweating. He had had a mild dry unproductive cough for 3 weeks. On examination he appeared to be in considerable pain. The pulse rate was 80/minute and the blood pressure 110/80 mm Hg. No abnormality was found in the cardiovascular system. The trachea was central, and there was evidence of a right pleural effusion. The abdominal muscular tone was normal, but there was tenderness in the right hypochondrium. There was no ascites, and no abdominal viscera or other masses were palpable.

Investigations showed the following: haemoglobin 10·7 g/100 ml, PCV 87 per cent, WBC 10 900/mm^3, serum bilirubin 0·6 mg/100 ml, thymol turbidity 2 units, zinc sulphate turbidity 6 units. Over the next 2 days he continued to complain of abdominal and chest pain, and there was deterioration in his condition. The serum amylase was now 7300 Somogyi units/100 ml, and chest X-ray showed a diffuse opacity in the right chest. On 20 April 900 ml of straw-coloured fluid were aspirated from the right chest, and a further 1000 ml on 22 April. The pleural fluid contained amylase, 73 600 Somogyi/100 ml. Between 19 April and 10 May the effusion was aspirated on six occasions, but without remission of his symptoms. In view of the rapid reaccumulation of the right pleural effusion an intercostal tube was inserted on 12 May and left *in situ* for 4 days, but after its removal further reaccumulation of fluid necessitated its reinsertion. In view of the failure of conservative therapy and increasing pain it was thought that a more aggressive form of treatment was required. During the 5 weeks of preoperative treatment, the serum amylase varied between 1100 and 7300 Somogyi u./100 ml while the pleural fluid amylase was markedly elevated at between 2900 and 278 000 Somogyi u./100 ml (*Table I*). The urinary amylase and diastase levels were also elevated. The pleural aspirate remained straw-coloured until 6 May, when it became dark brown.

Table I: SERUM AND PLEURAL FLUID AMYLASE LEVELS

Date	Volume of pleural fluid aspirated (ml)	Serum amylase (Somogyi u./100 ml)	Pleural fluid amylase (Somogyi u./100 ml)
19 April	—	7300	—
20 April	900	—	—
22 April	1000	—	73 600
24 April	—	4000	—
25 April	—	5700	200 000
28 April	750	—	—
29 April	1000	—	287 000
8 May	—	3000	—
10 May	820	—	—
12 May	Intercostal tube inserted for 4 days		33 000
15 May	—	—	34 200
21 May	Intercostal tube reinserted		
23 May	—	1100	—
24 May	—	1400	2 900
25 May	Subtotal pancreatectomy		
10 July	—	265	—
15 Oct.	—	205	—

On 17 May the urinary amylase was 1200 Somogyi u./100 ml. On 24 May the urinary diastase was 128 Wohlemuth units.

At laparotomy on 25 May 1974 adhesions were found between the omentum, the transverse colon and the anterior abdominal wall. There was no free fluid. The duodenum and head of the pancreas were adherent to the posterior abdominal wall, but neither cysts nor fistulous tracts were present. The gallbladder and the extrahepatic biliary tree were normal. No communication was found between the peritoneal and pleural cavities. A subtotal pancreatectomy was performed, leaving 1 cm of pancreas adjacent to the duodenal curve. The pancreatic duct showed a stricture at the ampulla of Vater. This was dilated and the distal end of the transected pancreas and its duct were implanted into the posterior surface of the stomach. The postoperative course was complicated by the pleural fluid becoming frankly purulent and by the development of a pleurocutaneous fistula after removal of the intercostal tube. Subsequent recovery was uneventful. The serum amylase level gradually returned to normal, being 305 Somogyi units when the patient was discharged 12 days later.

---

* Colombo General Hospital, Sri Lanka.

On histological examination the pancreas showed marked infiltration with thick bands of fibrous tissue which passed between the lobules. The fibrous tissue was mature with few fibroblasts and was infiltrated by chronic inflammatory cells, mainly lymphocytes and plasma cells. Many of the pancreatic ductules were dilated. A few of the ducts contained an inflammatory exudate with polymorphonuclear leucocytes. Some of the blood vessels showed endarteritis obliterans, and one blood vessel contained an infected thrombus. The remaining pancreatic tissue, both endocrine and exocrine, appeared normal.

When reviewed in October 1974 the patient appeared well and had had no further attacks of abdominal pain. The serum amylase was 205 Somogyi/100 ml.

Discussion

Pleural effusion is now recognized as a complication of acute pancreatitis. It usually occurs on the left, but may be bilateral (Lipp and Aaron, 1950; Roseman et al., 1960; Kaye, 1968). Similar features have been described with chronic relapsing pancreatitis (Mitchell, 1964; Miridjanian et al., 1969). The diagnostic significance of a high level of amylase in the pleural fluid was first described by Werner (1942), and since then Kaye (1968) has collected 37 such cases from the literature. Hammarsten et al. (1959) investigated 12 patients with pleural effusion which was not associated with pancreatic disease and found that, although the pleural amylase level was mildly elevated, it was always below the level of the serum amylase. They thought that a pleural fluid amylase level of over 200 Somogyi units was suggestive of pancreatic disease. More recently, Bellman and Rajaratnam (1974) have described 2 patients with perforation of the oesophagus in whom the pleural fluid amylase was elevated and above that of the serum amylase. They suggested that the enzyme was derived from the swallowed saliva.

The mechanism of formation of pleural effusions in pancreatic disease has been the subject of much interest. As in other acute upper abdominal lesions, the effusion could occur as a sympathetic effusion consequent upon an irritation of the diaphragm, but in such cases the enzyme content would not be elevated above the serum levels. Transmission of peritoneal fluid through the normal apertures in the diaphragm would imply the formation of a mediastinal pancreatic pseudocyst which had subsequently ruptured into the pleural cavity, but this has rarely been described. Blood-borne transfer of pancreatic enzymes is also unlikely, since in such cases there would be an equal incidence of pleural effusions on the two sides, and the amylase levels would be the same as in the serum. The greater incidence of left-sided pleural effusions has been explained by the more intimate relationship of the left hemidiaphragm with the pancreas. The frequency with which pseudocysts have been associated with pleural effusions has suggested the possibility of transdiaphragmatic rupture, which would account for the high amylase content in the pleural fluid (Hunt, 1954; Goldman et al., 1962). Such cases are, however, rare, the majority of pancreatic pseudocysts having no communication across the diaphragm (Hammarsten et al., 1959).

The presence of numerous lymphatic pathways between the upper abdominal and thoracic cavities and the rapid transfer of enzymes and particulate matter from the peritoneal cavity into the mediastinal lymph nodes and the thoracic duct in experimental animals suggest that pancreatic enzymes may reach the pleural fluid via the lymphatics in man (Cunningham, 1922; Perry, 1947). Pancreatic enzymes, on account of their large molecular weight, are unlikely to be transferred directly from the pancreas into the blood capillaries, and they may be carried in the lymph to the thoracic duct (Dumont et al., 1960).

Obstruction to the outflow of the pancreatic duct, as in the case reported here, increases the movement of pancreatic enzymes into the interstitial fluid, and thence into the lymphatics and the thoracic duct (Bartos et al., 1966). The theory of lymphatic transfer of pancreatic enzymes seems the most attractive of the various mechanisms that have been postulated to explain the accumulation of pancreatic enzymes in pleural effusions in pancreatitis. It would seem to be applicable to our patient, in whom no abnormal pathways across the diaphragm were demonstrated and in whom neither intraperitoneal free fluid nor pseudocyst was present. Obstruction at, or close to, the ampulla of Vater would have caused a maximal rise in intraductal pressure close to the ampulla, hence accounting for the formation of a right-sided pleural effusion.

Most of the reported cases with pleural effusions have been successfully managed on conservative lines, although thoracotomy and decortication have been necessary in some (Mitchell, 1964). In the present patient persistent abdominal symptoms and chest pain, together with the rapid reaccumulation of an enzyme-rich pleural effusion and deterioration in his general condition, prompted a more aggressive approach. Subtotal pancreatectomy was followed by complete relief of symptoms. It is possible that dilatation of the pancreatic duct would have sufficed and such a procedure may be worthy of trial.

Acknowledgement

We have pleasure in thanking Mrs Mohini Crossette-Thambyah for typing the manuscript.

References

BARTOS V., BRZEK V. and GROH J. (1966) Alterations in human thoracic duct lymph in relation to the function of the pancreas. *Am. J. Med. Sci.* **252**, 31–38.

BELLMAN M. H. and RAJARATNAM H. N. (1974) Perforation of the oesophagus with amylase rich pleural effusion. *Br. J. Dis. Chest* **68**, 197–201.

CUNNINGHAM R. S. (1922) Studies in absorption from serous cavities. IV. On the passage of blood cells and granules of different sizes through the walls of the lymphatics in the diaphragm. *Am. J. Physiol.* **62**, 248–252.

DUMONT A. E., DOUBILET H. and MULHOLLAND J. H. (1960) Lymphatic pathways of pancreatic secretion in man. *Ann. Surg.* **152**, 403–409.

GOLDMAN M., GOLDMAN G. and FLEISCHNER F. G. (1962) Pleural fluid amylase in acute pancreatitis. *New Engl. J. Med.* **266**, 715–716.

HAMMARSTEN J. F., HONSKA W. L. and LIMES B. J. (1959) Pleural fluid amylase in pancreatitis and other diseases. *Am. Rev. Tuberc.* **79**, 606–611.

HUNT R. S. (1954) Pancreatico-bronchial fistula. A report on two cases. *Br. J. Surg.* **41**, 599–603.

KAYE H. D. (1968) Pleuro-pulmonary complications of pancreatitis. *Thorax* **23**, 297–306.

LIPP W. F. and AARON A. H. (1950) Acute pancreatitis: further observations of value in its recognition. *NY State J. Med.* **50**, 2043–2047.

MIRIDJANIAN A., AMBRUOSO V. N., DERBY B. M. and TICE D. A. (1969) Massive bilateral haemorrhagic pleural effusions in chronic relapsing pancreatitis. *Arch. Surg.* **98**, 62–66.

MITCHELL E. E. (1964) Relapsing pancreatitis with recurrent pericardial and pleural effusions. *Ann. Intern. Med.* **60**, 1047–1053.

OCHSNER A. and DEBAKEY M. E. (1938) Sub-phrenic abscess: collective review and analysis of 3608 collected and personal cases. *Surg. Gynecol. Obstet.* **66**, 426–438.

PERRY T. T. (1947) Role of lymphatic vessels in the transmission of lipase in disseminated pancreatic fat necrosis. *Arch. Pathol.* **43**, 456–465.

ROSEMAN D. M., KOWLESSAR O. D. and SLEISENGER M. H. (1960) Pulmonary manifestations of pancreatitis. *New Engl. J. Med.* **263**, 294–296.

WERNER H. (1942) cited by KAYE (1968).

Br. J. Surg. Vol. 62 (1975) 563–564

Xanthogranulomatous pyelonephritis: a report of 2 cases

O. S. MORGAN, G. D. NICHOLSON, P. S. JOHNSON AND D. W. ATKINSON*

SUMMARY

Two cases of xanthogranulomatous pyelonephritis are reported in Negroes. The clinical findings are similar to those in previously reported cases. In 1 case nephrolithotomy was followed by the development of a perinephric abscess 8 months later. Late diagnosis has limited experience with more conservative management, which should be reserved for demonstrably focal disease.

XANTHOGRANULOMATOUS pyelonephritis is an infrequently occurring variant of pyelonephritis rarely reported in Negroes. In a review of 38 cases in whom ethnic origin was noted only 10 per cent occurred in Negroes (Anhalt et al., 1971). We report 2 cases of this condition in patients of African descent, in one of whom management by removal of the associated renal calculus was unsuccessful.

Case reports

Case 1: A 67-year-old housewife was admitted to the University Hospital, Kingston, after an 8-week period of increasing ill-health. During the previous 4 months she had experienced intermittent episodes of pain in the left flank and iliac fossa, accompanied by increased frequency of micturition. In the 4 weeks antedating admission she had complained of lassitude, chills, rigors and night sweats. She had lost over 13 kg in weight since the onset of her illness.

On examination a large non-tender irregular mass was palpable in the right hypochondrium. The urine contained many pus cells and a few red blood cells, but was sterile on culture. The haemoglobin was 8·6 g/100 ml, the white cell count 8100/mm^3 with a normal differential, and the ESR 100 mm in 1 hour. Blood cultures were sterile. The blood urea was 28 mg/100 ml and the plasma creatinine 1·0 mg/100 ml. An abdominal film revealed a large soft tissue mass in the left upper quadrant with a dense opacity within its borders. Intravenous pyelography showed only faint excretion of the dye on the left side. The left renal outline was enlarged and calicectasis was observed in the upper pole. No caliceal pattern was distinguishable in the lower pole which contained a large calculus. The right kidney functioned normally. At cystoscopy there was milky urine coming from the left ureter, whose orifice was grossly oedematous. A left retrograde pyelogram confirmed the presence of calicectasis. Pus obtained at this examination was sterile. At nephrectomy a large hydronephrotic kidney was found. The perinephric tissues were grossly oedematous and the kidney was adherent to the spleen and descending colon.

The kidney was 17 cm long and weighed 300 g. The calices were enormously distended by thin pus and there was fibrotic thickening of their walls. There was severe loss of renal parenchymal tissue. A large calculus 3 cm in diameter lay within a lower pole calix. Multiple yellow nodules measuring up to 2 cm in diameter were scattered throughout the solid areas of tissue (*Fig*. 1).

The histological appearances were of acute on chronic pyelonephritis with widespread xanthogranulomatous change. The renal parenchyma was almost entirely destroyed apart from a few remnant tubules containing hyaline casts. There was extensive fibrosis and scattered abscess formation. The dense infiltration of inflammatory cells included neutrophils, plasma cells and lymphocytes with follicle formation. In addition, abundant foamy histiocytes were present, often forming large aggregates. Oil-Red O stains confirmed these cells to be rich in cytoplasmic lipid. Very few giant cells were found (*Fig*. 2).

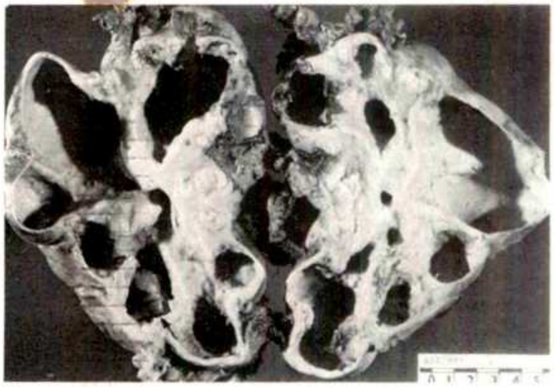


Fig. 1. *Case* 1. Photograph of the bisected kidney showing the grossly dilated caliceal system. The renal parenchyma is almost indistinguishable, being replaced by yellow nodules. The arrow points to the calculus in a lower pole calix.

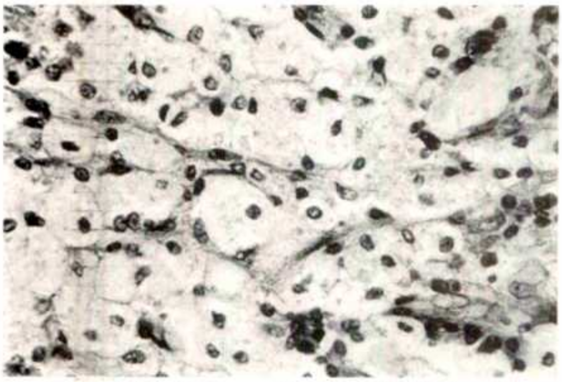


Fig. 2. *Case* 1. Photomicrograph showing lipid-laden histiocytes. (× 210.)

Case 2: A 51-year-old housewife was transferred to the University Hospital, Kingston, for investigation of a non-functioning left kidney. A large calculus had been removed from the left renal pelvis 8 months previously. Two months prior to admission she had been treated for a urinary tract infection and 2 weeks later had developed a left perinephric abscess which, although widely incised and drained, had continued to discharge.

On examination the patient seemed surprisingly well. She was afrebile. Large quantities of foul-smelling pus could be expressed from the left loin wound and yielded a mixed growth of *Staphylococcus pyogenes*, *Proteus* sp. and *Pseudomonas pyocyanea*. Intravenous pyelography showed a non-functioning left kidney; the right kidney was normal. Retrograde pyelography was unsuccessful. At operation a large pyonephrosis was found. The kidney was removed with difficulty from the surrounding tissues to which it was extremely adherent.

---

* Departments of Medicine, Surgery and Pathology, University of the West Indies, Mona, Kingston 7, Jamaica, West Indies.

The kidney was 12 cm long and weighed 150 g. The calices, which were dilated, had thickened walls and haemorrhagic mucosa. The renal parenchyma was greatly reduced, pale in colour and contained multiple yellow nodules of variable size, averaging 1 cm in diameter, and frequently bordering the calices. No calculi were found. There was severe acute on chronic pyelonephritis with extensive destruction of renal parenchyma and abscess formation. The inflammatory infiltrate contained numerous neutrophils, plasma cells and lymphocytes with follicle formation. Many foamy histiocytes forming large aggregates were present. These cells were rich in cytoplasmic lipid. An occasional multinucleate giant cell was also present.

Discussion

These cases are similar to those reported previously, in which the prominent features include an enlarged non-functioning kidney associated with renal calculi, obstruction and chronic infection. The interest in this condition lies in the importance of its differentiation from carcinoma and tuberculosis of the kidney on clinical, radiological and pathological grounds, permitting a planned approach to therapy.

Malek et al. (1972) have suggested the classification of xanthogranulomatous pyelonephritis into three stages. Our cases fall into stage III of this classification, with nephric, perinephric and paranephric involvement in which removal of the diseased kidney is the treatment of choice. The disease does not tend to recur after nephrectomy even following incomplete excision (Elliott et al., 1968; Malek et al., 1972), and this strongly suggests the pre-eminence of local rather than metabolic factors in its causation.

Anhalt et al. (1971) treated one of their patients with rare bilateral disease by nephrolithotomy with a favourable outcome. Our second case was treated by nephrolithotomy at a time when the diagnosis was unsuspected. The subsequent development of a perinephric abscess is indicative of persistent infection in that kidney. Diffuse involvement of the affected kidney has commonly preceded diagnosis and this has limited attempts at conservative management. Nephrolithotomy, alone or combined with partial excision, should be confined to the focal form of the disease in which absence of function is confined to the abnormal portion of the kidney (Mitchell et al., 1959). Non-function of the whole kidney, particularly where the associated calculus lies in a polar calix, should alert one to the possibility of diffuse disease. Until earlier diagnosis becomes possible, attempts at local excision will remain exceptional and total nephrectomy the established procedure for diffuse disease.

References

ANHALT M. A., CAWOOD C. D. and SCOTT R. (1971) Xanthogranulomatous pyelonephritis: a comprehensive review with report of 4 additional cases. *J. Urol.* **105**, 10–17.

ELLIOTT C. B., JOHNSON H. W. and BALFOUR J. A. (1968) Xanthogranulomatous pyelonephritis and perirenal xanthogranuloma. *Br. J. Urol.* **40**, 548–555.

MALEK R. S., GREENE L. F., DEWEERD J. H. and FARROW G. M. (1972) Xanthogranulomatous pyelonephritis. *Br. J. Urol.* **44**, 296–308.

MITCHELL R. E., DOBSON A. I. and KAY S. (1959) Xanthogranulomatous pyelonephritis. *Am. Pract. Dig. Treat.* **10**, 2150–2155.

NOW
MORPHINE
MINUS
VOMITING

CYCLIMORPH
TRADE MARK

CYCLIMORPH Injection has all the benefits of morphine plus an effective anti-emetic, cyclizine – in a single injection.

Cyclizine significantly reduces the incidence of nausea and vomiting,[1] whether associated with the condition or morphine-induced.

CYCLIMORPH is indicated in all conditions where morphine is needed.

[1] *Br. J. clin. Pharmac*, (1975), **2**, 81.

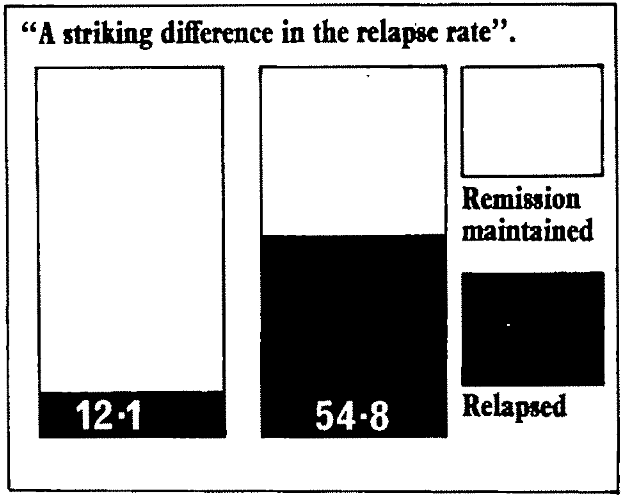
Full prescribing information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd.
Berkhamsted, Herts

"It is concluded that maintenance treatment of ulcerative colitis with sulphasalazine (salazopyrin) should be continued indefinitely unless contraindicated by side effects".[1]

The results of the above controlled trial carried out at the Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, are all the more welcome as earlier trials of cortisone[2] and prednisone[3] at standard dosages have shown them to be totally ineffective in reducing the number of recurrences of ulcerative colitis.

"Fortunately, Sulphasalazine tablets, 0.5 grams, 4 times a day will prevent relapses in the majority of patients with colitis, and only a few patients cannot tolerate this relatively small dose, which can be continued indefinitely, since we do not know when, if ever, it can be safely stopped".[4]



"A striking difference in the relapse rate".

"The patients who received dummy tablets had more than four times the relapse rate of those receiving sulphasalazine".[1] (Salazopyrin).

Salazopyrin (sulphasalazine) is available as the plain 0.5 g. tablet, 0.5 g. EN-tab and as an 0.5 g. suppository. Literature and detailed information on Salazopyrin are available on request.

References
1. Gut (1973) 14 923–926
2. Brit. med. J. (1959) 1 387–394
3. Lancet (1965) i 188–189
4. General Practitioner (1972) April 7 p 11.

Salazopyrin — to be continued indefinitely

Further information available from:—

Salazopyrin is a registered trade mark.

Pharmacia (Great Britain) Ltd.,
Paramount House,
75 Uxbridge Road,
London W5 5SS.
Telephone: 01-579 0102/7

Pharmacia

Br. J. Surg. Vol. 62 (1975) 565–566

An incision for *en bloc* nephrectomy

G. F. CASSIE*

SUMMARY

A surgical approach is described for en bloc removal of a large renal mass, enabling easy removal of such a mass with early palpation and ligation of the renal pedicle and with the minimum of assistance. The principle underlying the approach is that of detaching the costal margin and the free ribs from the abdominal musculature. In the experience of the author the wound always heals by first intention. No complications have been encountered and the patients have been discharged from hospital within 10 days of operation.

NEPHRECTOMY for a considerably enlarged kidney, in particular by malignant disease, commonly presents problems to the surgeon in his surgical approach. The standard loin incision with bridge or table break is unsuitable if the mass is large or the patient obese, as careful dissection of the pedicle becomes difficult, if not hazardous. The alternative thoraco-abdominal approach, which gives good exposure, is time-consuming and an additional burden to the patient, with increased time of anaesthesia and the risk of pulmonary complications.

During the past 8 years the author has used his approach on 8 occasions, 7 being for large hypernephroma masses and 1 for a huge myxoliposarcoma of the perinephric fat. On each occasion the wound has healed by first intention, no complications have been encountered and all the patients have left hospital within 10 days of operation. The principle underlying

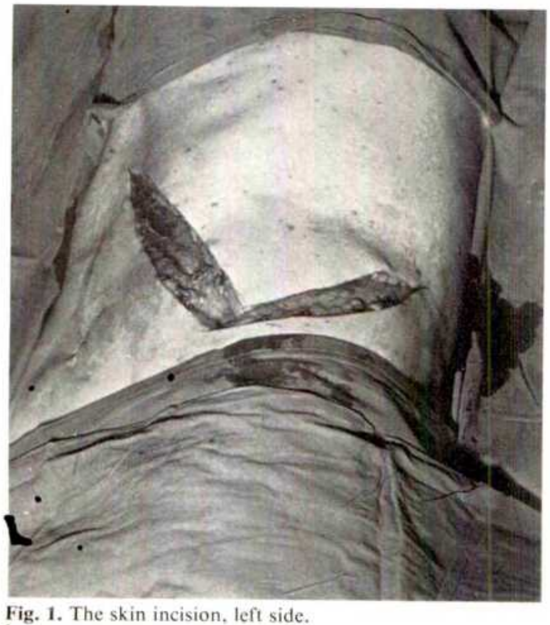


Fig. 1. The skin incision, left side.

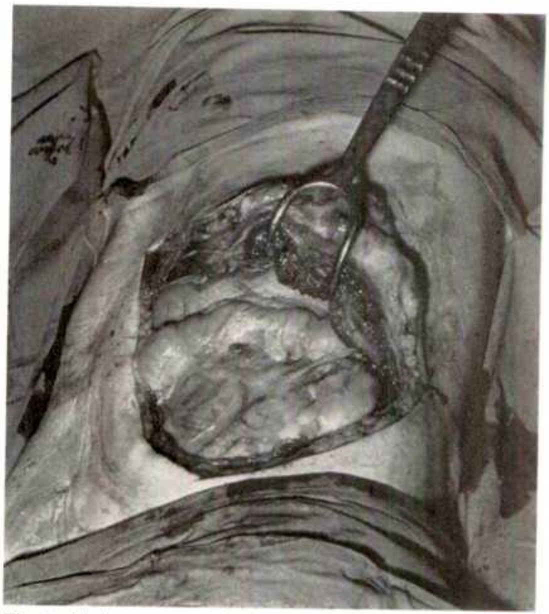


Fig. 2. Abdomen entered. The costal margin is elevated by a single retractor, displaying the splenic flexure of the colon overlying the renal mass.

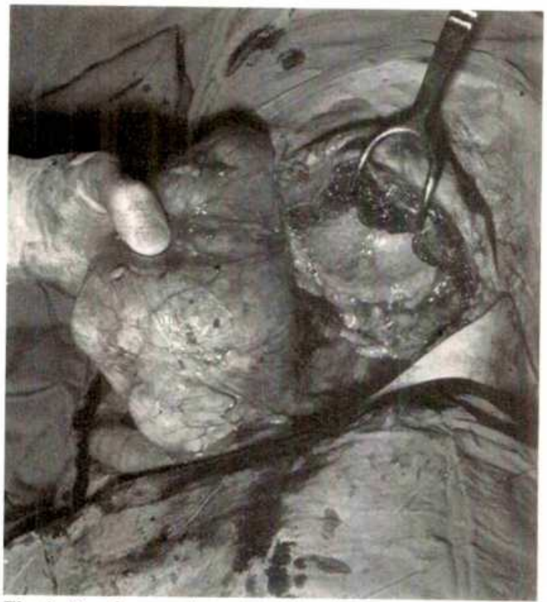


Fig. 3. Renal mass elevated *en bloc* from the posterior abdominal wall and rotated to the contralateral side to permit dissection and ligation of its pedicle.

---

* Queen Elizabeth II Hospital, Welwyn Garden City.

the approach requires the detachment of the costal margin and free ribs from the abdominal musculature, enabling an excellent exposure of the subdiaphragmatic area by elevation of the rib cage with one retractor.

The incision

The patients lies supine but tilted 45° to the opposite side by sandbags placed behind the scapula and buttock. The incision consists of a Kocher subcostal incision joined to a short incision into the loin just below the tip of the 11th rib (*Fig*. 1). The surgeon stands on the contralateral side. The muscles are cut by diathermy and the peritoneum entered (*Fig*. 2). A thorough examination of the abdominal contents can now be carried out. The flexure of the colon is stripped medially, displaying the renal mass within its perinephric capsule. This can now be elevated from the posterior abdominal wall (*Fig*. 3), enabling identification, inspection, palpation and ligation of the vascular pedicle. The adrenal is usually taken in the tissue block, its vessels being readily seen. The anterior and lateral peritoneum can be reconstituted during catgut suture of the abdominal wall with incorporation at the posterior end of a drain, which can be removed at 48 hours, the patient then being ambulant. Sutures are removed on the seventh day (*Fig*. 4). The huge solid tumour—a myxoliposarcoma—removed from the patient illustrated is shown in *Fig*. 5.

This approach is recommended to surgeons faced with removal of a large renal mass, as it permits a safe *en bloc* excision with the minimum of assistance. No mention of this incision is to be found in the standard texts on surgery or urology.

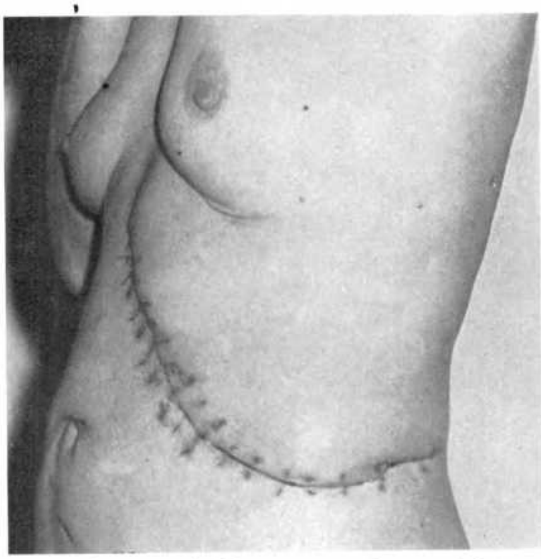


Fig. 4. After removal of the sutures on the seventh day.

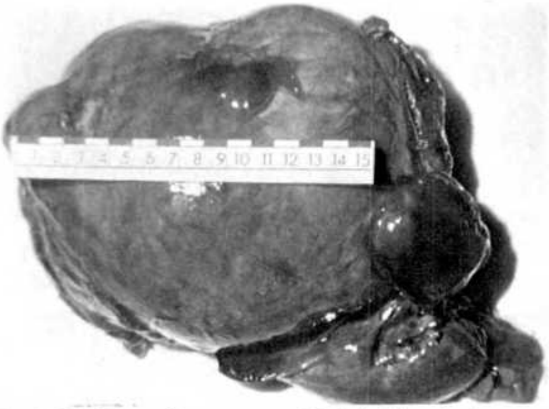


Fig. 5. The 20-cm diameter mass. The left kidney is shown projecting from the inferior aspect of the liposarcoma arising in the perinephric fat.

Acknowledgement

Thanks are due to Mr Marshall Potter, Queen Elizabeth II Hospital Photographer, for the illustrations.

Br. J. Surg. Vol. 62 (1975) 567–570

Undetected aorto-iliac insufficiency: a reason for early failure of saphenous vein bypass grafts for obstruction of the superficial femoral artery

D. CHARLESWORTH, P. L. HARRIS, F. D. CAVE AND LINDA TAYLOR*

SUMMARY

A series of 29 femoropopliteal bypass operations is described. The patients were selected carefully to exclude those with clinical and aortographic evidence of aorto-iliac disease. A pulsatility index was calculated from the velocity waveforms recorded over the common femoral and popliteal arteries. The pulsatility index is the ratio of the amplitude of the waveform to its mean height over one cardiac cycle. There was a highly significant difference in the result of the operation between patients with a pulsatility index of 4 or more in the common femoral artery and patients with a pulsatility index of less than 4. We concluded that calculation of this pulsatility index provides useful additional evidence when selecting patients suitable for a femoropopliteal bypass.

VARIOUS methods of reconstructing the superficial femoral artery have been tried in patients with chronic ischaemia of the lower limb and symptoms of intermittent claudication or pre-gangrene. There is little doubt that at present a reversed saphenous vein bypass graft is the most effective method of reconstruction when the superficial femoral artery is occluded (Szilagyi et al., 1964; Gutelius et al., 1965; DeWeese et al., 1966; Baddeley et al., 1970; DeWeese and Rob, 1971; Imperato et al., 1973; Watt et al., 1974), but even in the most experienced hands the operation is not an unqualified success. Most surgeons report that approximately one-third are occluded within 2 years of operation. When the operation is done for pre-gangrene or gangrene the failure rate is between 50 and 70 per cent (Tibbs, 1960; Taylor, 1962). The yearly failure rate in a group of our patients who had a femoropopliteal vein bypass and were followed up for 4 years is shown in *Fig*. 1. The majority of grafts occlude shortly after operation and it is obvious that it is not progression of disease which is responsible. Provided that the vein exceeds 4 mm in diameter and the operation is performed skilfully, it is probable that success or failure depends upon an adequate flow of blood into the graft from the common femoral artery and an adequate outflow into the tibial vessels—'run-off'. Measurement of run-off in the lower leg before operation has been attempted by several methods but the results have had little influence on the selection of patients for operation (Agrifoglio et al., 1961; Lassen et al., 1964; Dahn, 1965; Strandness and Bell, 1965; Mundth et al., 1969; Yao et al., 1970). In patients with a significant pressure drop along the iliac arteries a reconstruction of the iliac artery performed in conjunction with the femoropopliteal bypass graft increased the chances of the graft remaining patent. This information was obtained by direct recording at the time of operation (Moore and Hall, 1971). Similar information can be obtained before operation from waveform analysis of ultrasound signals and this information can be obtained non-invasively. We have studied the velocity waveforms in a series of 29 consecutive patients with occlusion of the superficial femoral artery, all of whom had a reconstruction using a reversed saphenous vein bypass graft.

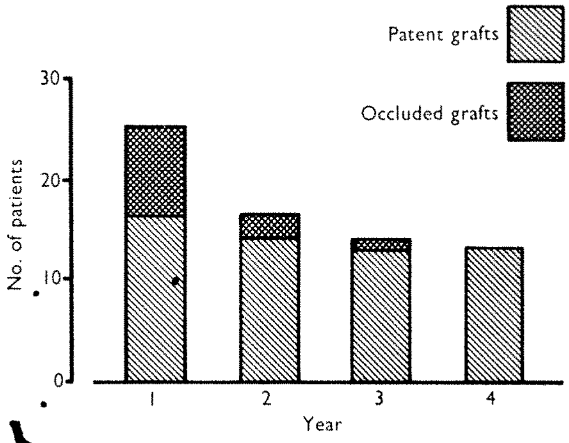


Fig. 1. Histogram showing a group of 25 patients who had a femoropopliteal bypass and were followed up for 4 years. The numbers of grafts which occluded in each year is shown as cross hatched.

Patients and methods

The investigation was carried out on a carefully selected group of patients with arteriosclerosis who had either symptoms of intermittent claudication of sufficient severity and duration to interfere seriously with their activities or pre-gangrene. Patients who had clinical evidence of aorto-iliac disease were excluded. The remaining patients were admitted to hospital for an aortogram, and X-rays were taken of the entire arterial tree from the aorta to the ankles. Patients with radiographic evidence of aorto-iliac stenosis or occlusion were treated by reconstruction of that segment and were not included in this series. Only patients whose arteriograms showed a complete occlusion of the superficial femoral artery and arteriographic grade 0 or 1 disease in the aorto-iliac segment were selected for a femoropopliteal bypass

---

* Department of Surgery, University Hospital of South Manchester.

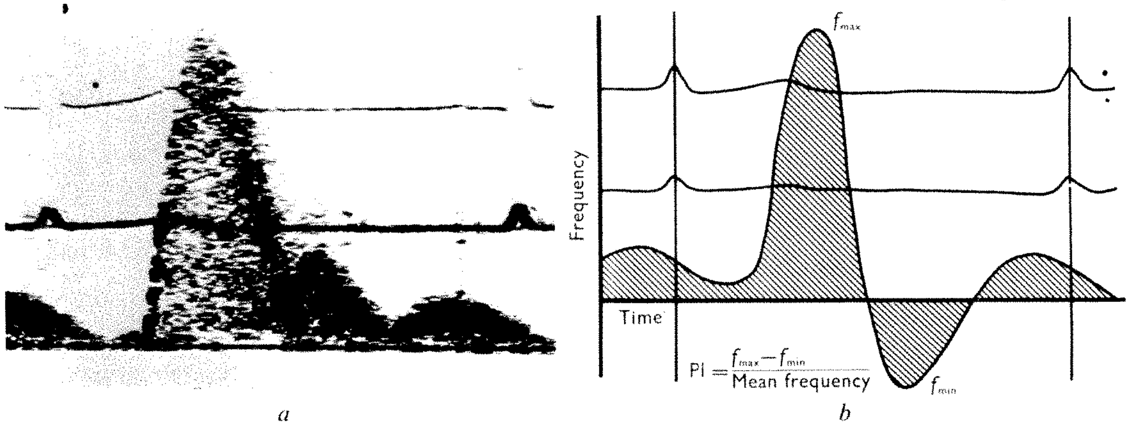


Fig. 2. *a*, Sonagram obtained from the common femoral artery of a healthy young man. *b*, Diagrammatic representation of the sonagram. The second peak in the velocity wave has been drawn below the base line to indicate reversed flow. Pulsatility index is calculated from amplitude ($f_{max} - f_{min}$) divided by mean frequency (height).

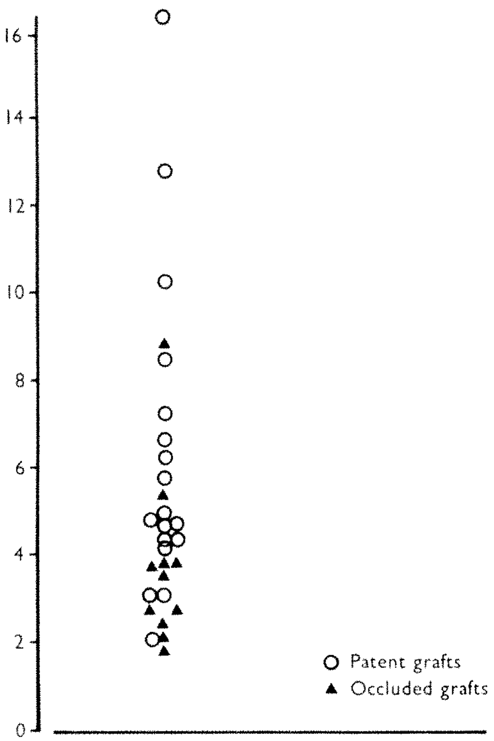


Fig. 3. Pulsatility index in the common femoral artery of a group of 29 patients compared with the early results of operation.

Table I: RESULTS OF OPERATION IN 8 PATIENTS WITH PRE-GANGRENE COMPARED WITH THE COMMON FEMORAL PULSATILITY INDEX (PI)

	PI	
	>4	<4
Number of patients	2	6
Graft patent after 6 months	2	1
Graft occluded within 6 months	0	5

Table II: RESULTS OF OPERATION IN 29 PATIENTS COMPARED WITH THE COMMON FEMORAL PULSATILITY INDEX

	PI	
	>4	<4
Number of patients	17	12
Graft after 6 months	15	3
Graft occluded within 6 months	2	9

(Harris et al., 1973, 1974). No attempt was made to select patients for operation on the basis of run-off. If the X-ray showed that the popliteal artery was patent the operation was considered to be technically possible.

Twenty-nine patients were studied, 23 male and 6 female, with an average age of 58·5 years (range 44–79 years). Twenty-one of the operations were for intermittent claudication and 8 were for pre-gangrene. Velocity waveforms were recorded from the common femoral, popliteal and tibial arteries of each patient before operation and again 6 months afterwards. The velocity waveforms were displayed as a sonagram and characterized by a single figure, the pulsatility index (*Fig.* 2) (Gosling et al., 1972; Harris et al., 1974). A subjective assessment of the result of each operation was made from the patient's symptoms. The results of preoperative measurements of pulsatility were compared with the subsequent results of the operation. All the operations were carried out by the same surgeon, and exactly the same technique was used in every patient.

Results

There were 21 patients with symptoms of intermittent claudication. Fifteen of these patients had a pulsatility index of 4 or more in the common femoral artery on the affected side, and 6 had a pulsatility index of less than 4. Thirteen (87 per cent) of the 15 patients who had a femoral pulsatility index of 4 or more had patent vein bypass grafts after an interval of 1 year. Eight patients had pre-gangrene and only 2 of these had a pulsatility index greater than 4 in the common femoral artery on the affected side. Both of these patients had a patent graft at follow-up (*Table I*). A total of 17 patients had a pulsatility index greater than 3·9 in the common femoral artery, and 15 (88 per cent) of these had patent vein bypass grafts at follow-up. In 12 patients the pulsatility index in the common femoral artery on the affected side was less than 4, and only 3 (25 per cent) had a patent graft at follow-up (*Table II*, *Fig.* 3).

Preoperatively the pulsatility index in the ipsilateral popliteal arteries was 1·9 ± 1·0 (normal range 9·4 ± 3·5) and in the posterior tibial arteries it was 1·6 ± 0·94 (normal range 8·3 ± 3·0). When the operation was successful the pulsatility index in the popliteal artery and posterior tibial artery increased invariably (*Fig.* 4). The mean pulsatility index in the popliteal artery rose from 1·9 to 6·8 (Student's t-test, $P < 0{\cdot}001$) after operation, and in the tibial artery it rose from 1·8 to 4·9 (Student's t-test, $P < 0{\cdot}001$).

Discussion

The patients who were included in this study were selected for a vein bypass operation without reference to the results of the pulsatility measurements. Patients who had angiographic evidence of disease in the aorto-iliac segment were excluded from the study and had a reconstruction of this segment in preference to a femoropopliteal vein bypass graft. No attempt was made to select patients on the basis of assessment of run-off; if the popliteal artery was visible on the angiogram a graft was considered to be technically possible. We divided the patients into two groups on the basis of the common femoral pulsatility index. The lower limit of pulsatility in the common femoral artery is 4 in normal volunteers and we regard values of less than 4 to be indicative of disease in the aorto-iliac segment (Harris et al., 1974). Patients with angiographic evidence of aorto-iliac stenosis were eliminated by the preoperative selection process, and consequently the 12 patients who had a pulsatility index of less than 4 in the common femoral artery had disease in the iliac arteries, the severity of which was not apparent on the angiograms. In general, there is a good correlation between angiographic appearances and the pulsatility index, but velocity waveform analysis can detect disease which is not apparent on single-plane angiograms (Harris et al., 1974).

There was a highly significant difference between the results in the patients with a normal common femoral pulsatility and those with an abnormal one ($P < 0{\cdot}003$, χ^2 test). A high percentage (88 per cent) of the patients who had claudication only and a normal pulsatility index in the common femoral artery had a patent graft after an interval of 12 months from the operation. The vein bypass graft occluded early in only 2 patients out of the 17 who had normal pulsatility indices. Both of these had angiographic evidence of poor run-off; in one none of the tibial vessels was patent, and in the other only one tibial artery was patent and the others were absent. We were unable to demonstrate any correlation between the pulsatility index measured in the popliteal artery or the posterior tibial arteries and the result of a vein bypass operation. The extent to which an arterial velocity wave is damped between the knee and the ankle can be assessed from the ratio of the pulsatility index in the popliteal artery to the pulsatility index in the posterior tibial arteries (Gosling et al., 1972). This value did not correlate well with the result of the operation and it did not prove to be a useful measure of run-off. The value of the pulsatility index at these two sites did give a good indication of whether a graft was patent and it provided a useful objective measurement when assessing patients at follow-up. Our results are in accord with previous clinical experience, in that the flow of blood into a femoropopliteal bypass is more important than run-off (Linton and Darling, 1962; Mavor, 1973; Horton, 1974).

The implication of these results is that patients who are selected for a femoropopliteal vein bypass operation on the basis of their clinical symptoms and angiograms should also have a pulsatility index of more than 3·9 in the common femoral artery in order to stand the best chance of success. When the pulsatility index on the side of the proposed operation is less than 4 it is now our practice to explore the aorto-iliac segment. We anticipate that this will yield more information about the influence of this segment of the arterial tree on the outcome of a femoropopliteal bypass graft.

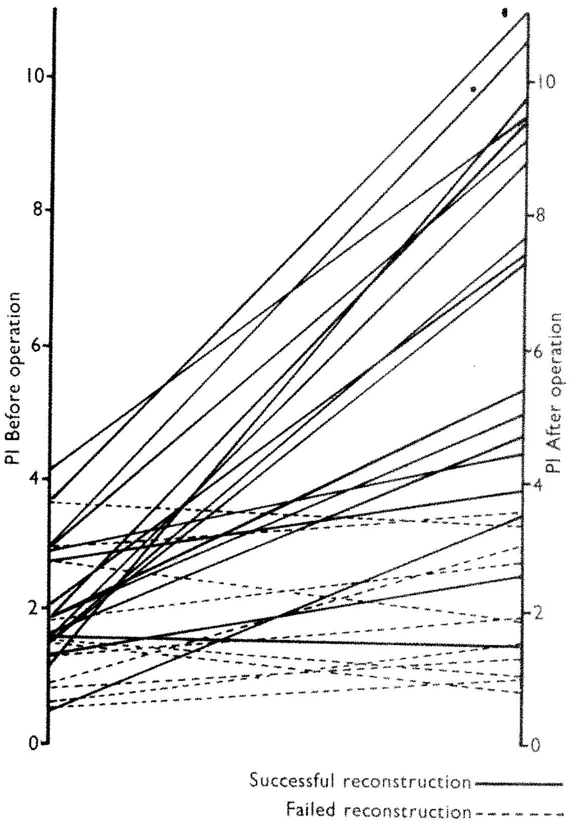


Fig. 4. Comparison between the pulsatility index in the popliteal artery before and after operation.

References

AGRIFOGLIO G., THORBURN G. D. and EDWARDS E. A. (1961) Measurement of blood flow in human lower extremity by indicator-dilution method. *Surg. Gynecol. Obstet.* **113**, 641–645.

BADDELEY R. M., ASHTON F., SLANEY G. and BARNES A. D. (1970) Late results of autogenous vein by-pass grafts in femoro-popliteal arterial occlusion. *Br. Med. J.* 1, 653–656.

DAHN I. (1965) On clinical use of venous occlusion plethysmography of calf: II. Results in patients with arterial disease. *Acta Chir. Scand.* **130**, 61–75.

DEWEESE J. A., BARNER H. B., MAHONEY E. B. and ROB C. G. (1966) Autogenous by-pass grafts and thromboendarterectomies for atherosclerotic lesions of the femoro-popliteal arteries. *Ann. Surg.* **163**, 205–214.

DEWEESE J. A. and ROB C. G. (1971) Autogenous venous by-pass grafts five years later. *Ann. Surg.* **174**, 346–355.

GOSLING R. G., KING D. H. and NEWMAN D. L. (1972) Blood velocity waveforms in the evaluation of atheromatous changes. In: ROBERTS V. C. (ed.) *Blood Flow Measurement.* London, Sector Publishing, p. 33.

GUTELIUS J. R., KREINDLER S. and LUKE J. C. (1965) Comparative evaluation of autogenous vein by-pass graft and endarterectomy in superficial femoral artery reconstruction. *Surgery* **57**, 28–35.

HARRIS P. L., TAYLOR L., CAVE F. D. and CHARLESWORTH D. (1974) The relationship between Doppler ultrasound assessment and angiography in occlusive arterial disease of the lower limbs. *Surg. Gynecol. Obstet.* **138**, 911–915.

HARRIS P. L., TAYLOR L., CAVE F. D., NAYLOR G. P., WILLIAMS P. C. and CHARLESWORTH D. (1973) The relationship between Doppler ultrasound assessment and angiography in occlusive arterial disease of the lower limbs. *Br. J. Surg.* **60**, 914.

HORTON R. E. (1974) Use of reversed saphenous vein graft in the treatment of pregangrene. *Ann. R. Coll. Surg. Engl.* **54**, 165–175.

IMPERATO A. M., BRACCO A. and KIM G. E. B. (1973) Comparisons of three techniques for femoro-popliteal arterial reconstruction. *Ann. Surg.* **177**, 375–380.

LASSEN N. A., HOEDT-RASMUSSEN K., LINDEBJERG I., PEDERSON F. and MUNCK O. (1964) Muscle blood flow determined by use of xenon 133. *Scand. J. Clin. Lab. Invest.* **15**, Suppl. 76, 61.

LINTON R. R. and DARLING R. C. (1962) Autogenous saphenous vein bypass grafts in femoro-popliteal obliterative arterial disease. *Surgery* **51**, 61–71.

MAVOR G. (1973) Results of reversed saphenous vein by-pass for femoro-popliteal experience. Paper presented to Vascular Surgery Society, October 1973.

MOORE W. S. and HALL A. D. (1971) Unrecognised aorto-iliac stenosis. *Arch. Surg.* **103**, 633–638.

MUNDTH E. D., DARLING R. C., NORAN J. M., BUCKLEY M., LINTON R. R. and AUSTEN W. G. (1969) Quantitative correlation of distal arterial outflow and patency of femoro-popliteal reversed saphenous vein graft with intraoperative flow and pressure measurements. *Surgery* **65**, 197–206.

STRANDNESS D. E. jun. and BELL J. W. (1965) Peripheral vascular disease: diagnosis and objective evaluation using a mercury strain gauge. *Ann. Surg.* **161**, 3–31.

SZILAGYI D. E., SMITH R. F. and ELLIOTT J. P. (1964) Venous allografts in femoro-popliteal arterioplasty. *Arch. Surg.* **89**, 113–125.

TAYLOR G. W. (1962) Arterial grafting for gangrene. *Ann. R. Coll. Surg. Engl.* **20**, 168–186.

TIBBS D. G. (1960) Arterial replacement and reconstruction. *Lancet* **2**, 1313–1318.

WATT J. K., GILLESPIE G., POLLOCK J. G. and REID W. (1974) Arterial surgery in intermittent claudication. *Br. Med. J.* **1**, 23–26.

YAO S. T., GOURMOS C. and HOBBS J. J. (1970) Evaluation of occlusive arterial disease of the lower extremities by an ultrasonic flow detection technique. *Br. J. Surg.* **57**, 382.

Br. J. Surg. Vol. 62 (1975) 571–572

Ossification in extradural fat in Paget's disease of the spine

PATRICK R. R. CLARKE AND H. I. WILLIAMS*

SUMMARY

A case of cauda equina compression by ossification in extradural fat at a level above the site of Paget's disease in a vertebra is described. Good recovery followed laminectomy and exposure of the dura mater.

DYSFUNCTION of the spinal cord or the cauda equina in cases of Paget's disease of vertebrae is well recognized. The causes of this (Sadar et al., 1972) are usually thought to be compression by bone, fracture dislocation or vascular occlusion. In this paper we describe a case in which the cauda equina was compressed by spicules of bone in extradural fat at a level slightly above the site of the vertebra which was affected by Paget's disease.

Case report

A 52-year-old quantity surveyor had complained of low back pain, particularly after physical exertion, for 12 years. He was admitted to the Neurosurgical Unit of Middlesbrough General Hospital on 15 January 1974 because of progressive weakness of the left leg of 3 months' duration. His walking was affected to the extent that he could hardly hobble around his house. Examination showed 3 cm of wasting of the left thigh, weakness of the flexors of the left knee joint, a depressed left knee jerk and absence of the left ankle jerk. There was no sensory loss. Radiographic examination (*Fig.* 1) revealed Paget's disease of the 3rd lumbar vertebra. Urinary hydroxyproline excretion was 12 mg in 24 hours. The level of alkaline phosphatase in the serum was 19·6 KA u./100 ml. Myelography was performed by the cisternal route, as an attempt at lumbar puncture had been unsuccessful. This investigation showed (*Fig.* 2) a total block at the level of the 2nd lumbar vertebra. On 30 January 1974 laminectomy of the 2nd and 3rd lumbar vertebrae was performed. The bone of the 3rd lumbar vertebra was soft and very vascular. At the 2nd lumbar vertebral level the extradural fat was abnormally firm and was indenting the dura mater. The fat at the 3rd lumbar level appeared normal to the naked eye. Exposure of the theca was achieved by removal of the extradural fat.

Histological examination of the bone of the 3rd lumbar vertebra (*Fig.* 3) showed the characteristic changes of Paget's disease. The extradural fat from the 2nd lumbar level (*Fig.* 4) contained fibrous tissue and spicules of newly formed bone.

Progress after operation was smooth. The left leg rapidly became stronger, and 6 weeks after surgery the patient was able to walk a mile at a reasonable speed.

Discussion

The interest in this case before operation lay in the fact that the obstruction to downward flow of Myodil was at the level of the 2nd lumbar vertebra, whereas the Paget's disease appeared radiologically to be confined to the 3rd lumbar vertebra. Sarcomatous change and extension into the extradural space were considered as a possible explanation of this. The operative and histological findings, however, made it clear that the cause of the compression of the theca was ossification in the extradural fat. The literature on neurological dysfunction in Paget's disease of the vertebral column has recently been reviewed by Sadar et al. (1972), who added 4 cases of their own to the 86 reported by previous authors. In the same year Cartlidge et al. (1972) described 3 further cases. As far as we are aware, ossification in extradural fat in this condition has not previously been reported. Subperiosteal bone spiculation is, on the other hand, well recognized (Direzke and Milnes, 1970). According to Klenerman (1966) the dura mater is densely adherent to the adjacent bone in Paget's disease of the spine, but this was not our experience in the present case.

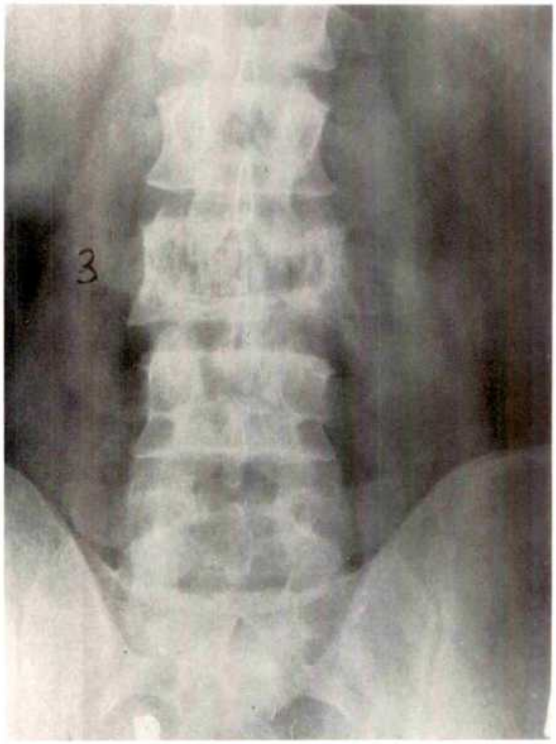


Fig. 1. Radiograph showing Paget's disease of the 3rd lumbar vertebra.

Although severe neurological deficit associated with Paget's disease of the spine makes surgery necessary, the place in the future of calcitonin M therapy both as a primary treatment and as a prophylactic against recurrence will need to be considered. Falls in serum alkaline phosphatase levels during calcitonin therapy have been held (Woodhouse et al., 1971) to be due to a reduction in the number or activity of osteoblasts.

---

* Departments of Neurosurgery and Pathology, Middlesbrough General Hospital.

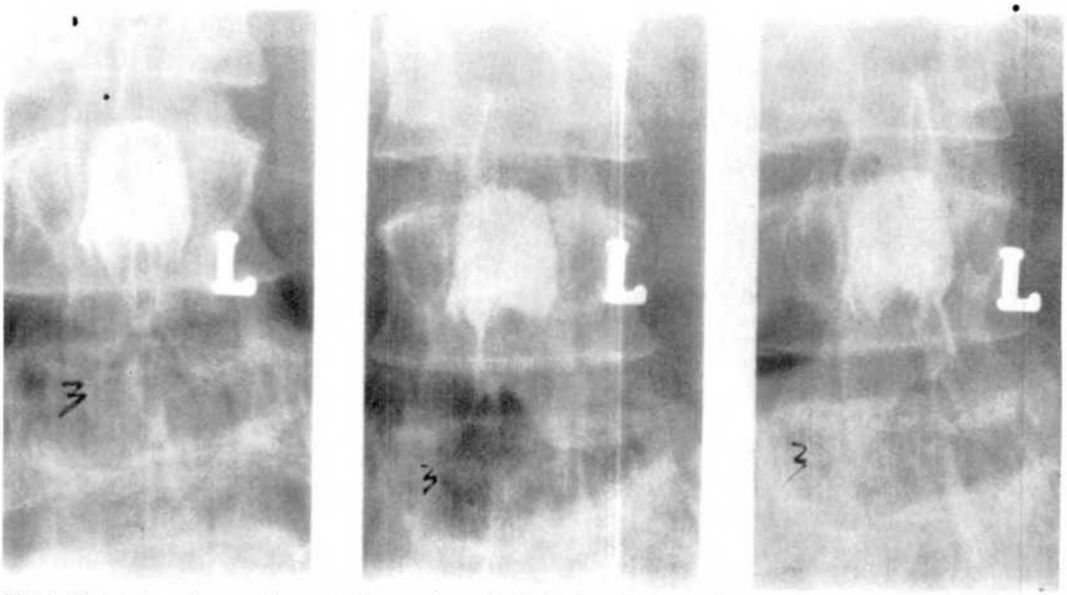


Fig. 2. Cisternal myelogram demonstrating a subarachnoid block at the level of the 2nd lumbar vertebra.

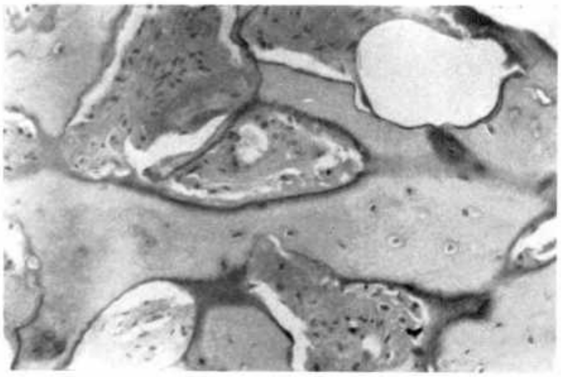


Fig. 3. Bone from the 3rd lumbar vertebra showing changes of Paget's disease. (× 63.)

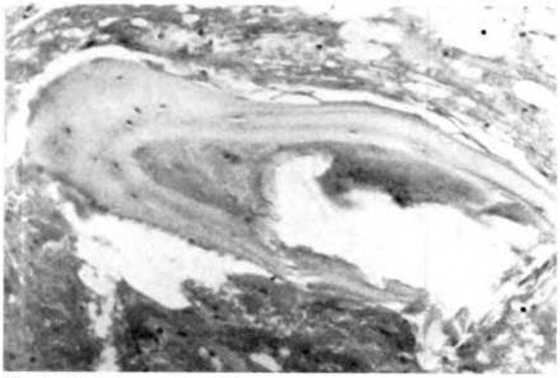


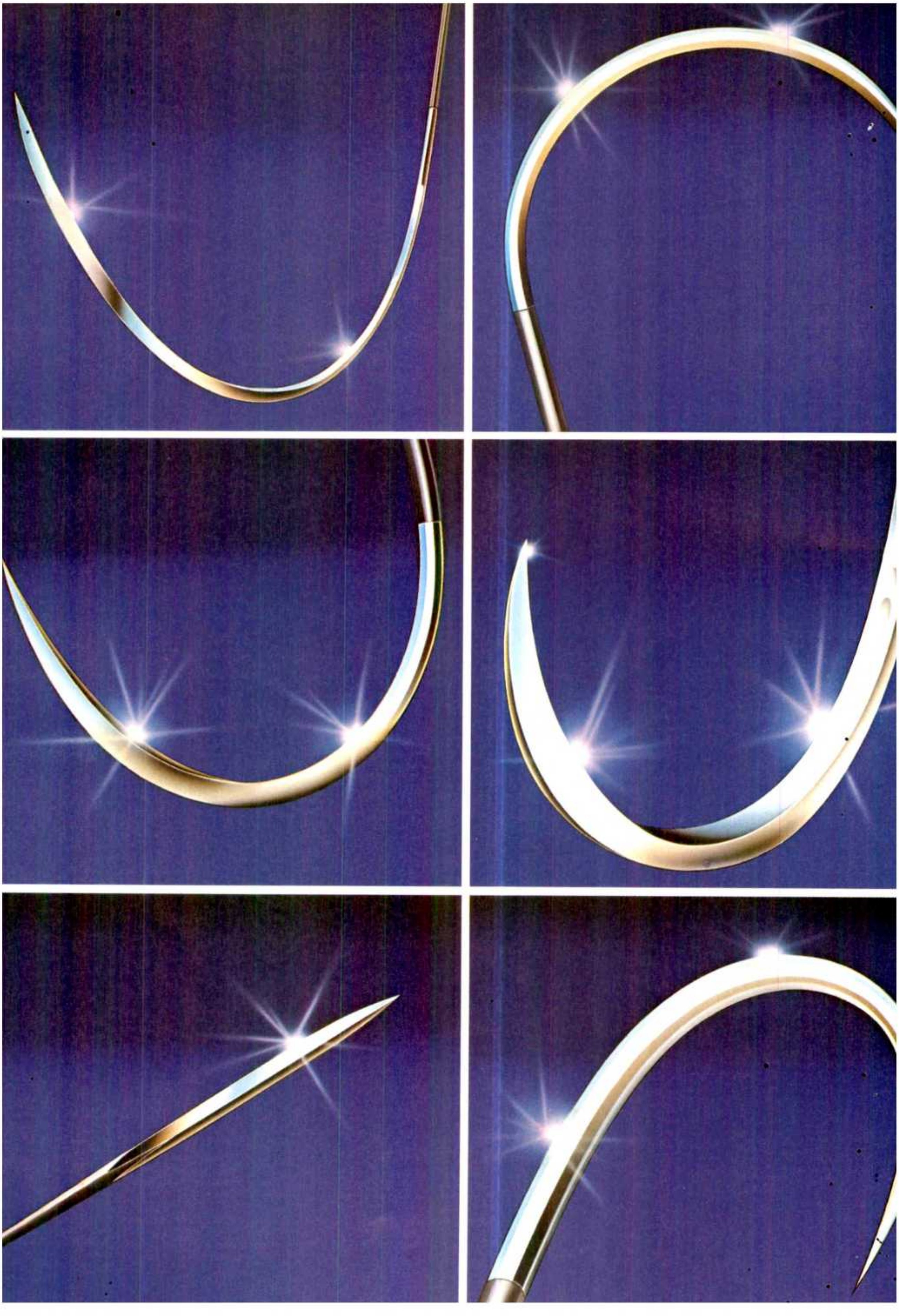
Fig. 4. Spinal extradural fat containing a bone spicule. (× 63.)

References

- CARTLIDGE N. E. F., MCCOLLUM J. P. K. and AYYAR R. D. (1972) Spinal cord compression in Paget's disease. *J. Neurol. Neurosurg. Psychiatry* **35**, 825–828.
- DIREZKE M. and MILNES J. N. (1970) Spinal cord compression in Paget's disease. *Br. J. Surg.* **57**, 239–240.
- KLENERMAN L. (1966) Cauda equina and spinal cord compression in Paget's disease. *J. Bone Joint Surg.* (*Br.*) **48**, 365–370.
- SADAR E. S., WALTON R. J. and GOSSMAN H. H. (1972) Neurological dysfunction in Paget's disease of the vertebral column. *J. Neurosurg.* **37**, 661–665.
- WOODHOUSE N. J. Y., BONDIER PH., FISHER M., JOPLIN G. F., REINER M., KALU D. N., FOSTER G. V. and MACINTYRE, I. (1971) Human calcitonin in the treatment of Paget's bone disease. *Lancet* **1**, 1139–1143.

the range is ours
the choice is yours

ETHICON
TRADEMARK
Eyeless needled sutures



WE MAKE SOME VERY IMPORTANT POINTS

ETHICON* Eyeless Needled Sutures offer three outstanding advantages over traditional eyed needles.

Point 1 A new sharp needle every time.

Point 2 Reduced trauma–with ETHICON eyeless needles there is no large eye and only one strand of material to pass through tissue.

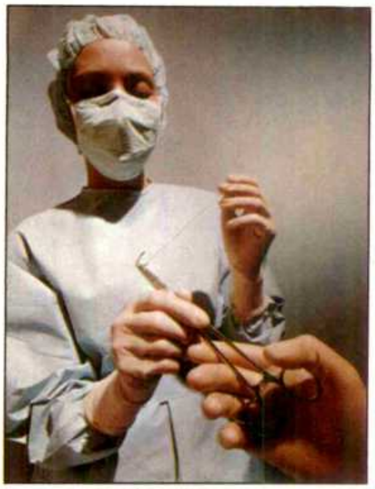
Point 3 Consistent high quality–by precisely controlled manufacture of a complete sterile suture in a single package.

The choice is yours

Most surgeons agree that there is no universal suture. Most probably there never will be. Each patient, each procedure, and each layer of tissue differs from the next. This is why we at ETHICON manufacture such a comprehensive range of eyeless needled sutures.

You can choose from our wide selection of materials, absorbable and non-absorbable, securely attached to a stainless steel needle of your choice. The consistent high quality of ETHICON eyeless needled sutures provides predictable performance. This enables you to concentrate on the most critical aspect of your surgery–the well-being of the patient.

© ETHICON LTD 1974* Trade Mark



Reduce Trauma

Quality and Reliability at every stage

ETHICON
TRADEMARK
Eyeless needled sutures

Widest range. Finest quality

ETHICON Ltd., Bankhead Avenue, Edinburgh EH11 4HE, Scotland

PROLENE* Monofilament polypropylene
for security you can count on

When the reliability of a non-absorbable is required in a contaminated or potentially contaminated field many surgeons are now choosing PROLENE suture. Made from polypropylene, a material of relative biological inertness, monofilament PROLENE suture is not degraded by tissue enzymes and is virtually unaffected by the presence of infection.

Security for extended approximation

Where wound healing may be delayed PROLENE suture can be relied on to retain its tensile strength.

Secure knot-holding

PROLENE suture is able to deform and flatten on knotting to give knot security superior to any other monofilament.

Security through reduced risk of suture extrusion and sinus formation

The specially smooth monofilament structure of PROLENE suture and its ability to tolerate infection extremely well can lessen the risk present with a braided suture in a contaminated wound.

Indications: PROLENE Polypropylene suture may be used wherever a non-absorbable surgical suture is recommended.

Precautions: Unused PROLENE sutures may not be autoclaved more than three times by the standard autoclaving method without loss of strength. Care should be taken to avoid damaging the surface of the material with surgical instruments.

ETHICON

Widest range. Finest quality

© ETHICON LTD 1974* Trade Mark

ETHICON LTD. Bankhead Avenue, Edinburgh EH11 4HE, Scotland.

Br. J. Surg. Vol. 62 (1975) 573–575

Nodular fasciitis: an unusual cause of extradural spinal cord compression

R. P. SENGUPTA, S. C. SO AND R. H. PERRY*

SUMMARY

A case of nodular fasciitis causing extradural spinal cord compression with a successful outcome following removal is reported. Such a tumour within the spinal cord has never been reported. The pathogenesis of a nodular fasciitis in this situation and its differential diagnosis is discussed.

NODULAR fasciitis is a well-recognized tumour occurring in the subcutaneous tissues over the trunk and limbs but has never been observed in the spinal canal. The following is a case report of such a tumour arising in the extradural space and causing spinal cord compression.

Case report

A 64-year-old retired schoolteacher was admitted to the Regional Neurological Centre in January 1974 with a 1-month history of lower thoracic back pain. It was constant and radiated to the right hypochondrium. Three weeks before admission he had noticed that he was unsteady on walking and that his legs had become weak. Shortly afterwards he developed hesitancy and urgency of micturition. Two days before admission he was unable to walk. For the past 8 years he had had hypertension and 2 years previously had had a cerebrovascular accident causing a left hemiparesis.

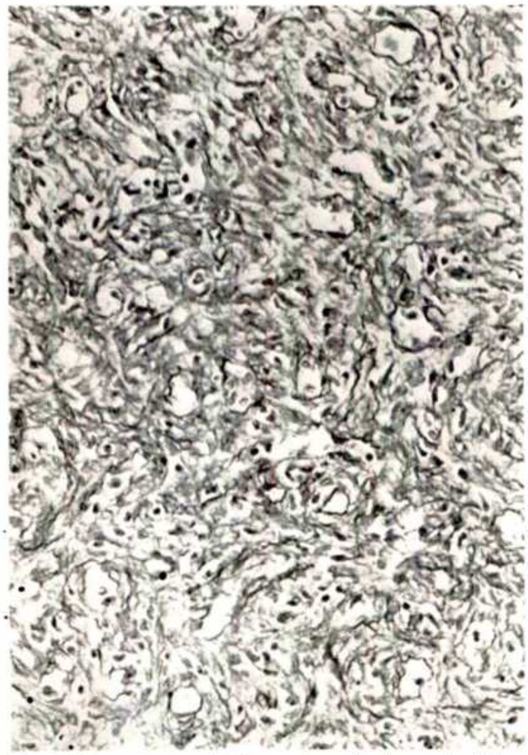


Fig. 1. Photomicrograph illustrating a haphazard cellular arrangement with reticulin fibres outlining cells and demarcating vascular spaces. Reticulin. (× 120.)

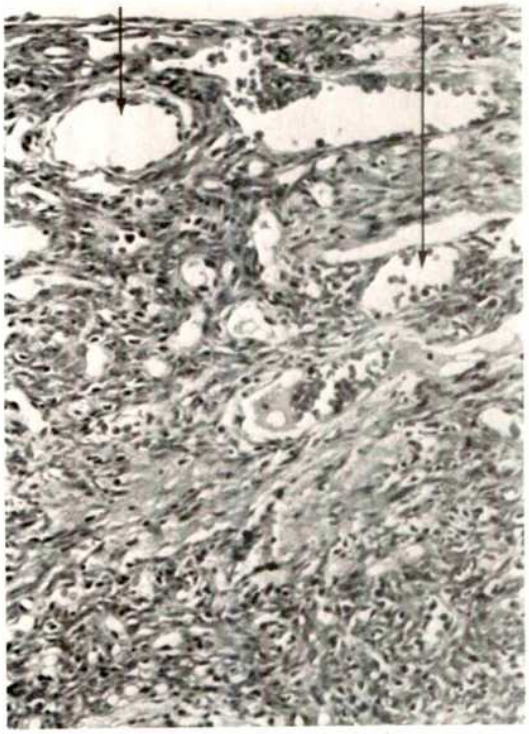


Fig. 2. Photomicrograph illustrating marked vascularity of the edge of the lesion. Arrows point to vascular spaces. HE. (× 160.)

On examination the patient had a localized tenderness over the spine of D9. Marked weakness was present in both lower limbs involving all muscle groups. There was no wasting, the tone was increased with brisk reflexes and the plantar responses were extensor. Pain and temperature sensation below the level of D9 were impaired. Both position and vibration sensations were absent below the hip joint and Romberg's sign was positive. He was hypertensive (220/130 mm Hg) with retinal vascular changes and left ventricular voltage changes on the ECG. Plain X-rays of the spine were normal. Myelography showed a complete block at D9 with features suggesting an extradural tumour. The cerebrospinal fluid protein was 76 mg per cent.

At operation the laminae from D8 to D11 were removed. A firm lobulated tumour was found in the extradural space pushing the cord anteriorly. The tumour was not attached to the dura or any nerve root. It was only loosely attached to

---

* Department of Neurosurgery and Neuropathology, Regional Neurological Centre, Newcastle General Hospital, Newcastle upon Tyne.

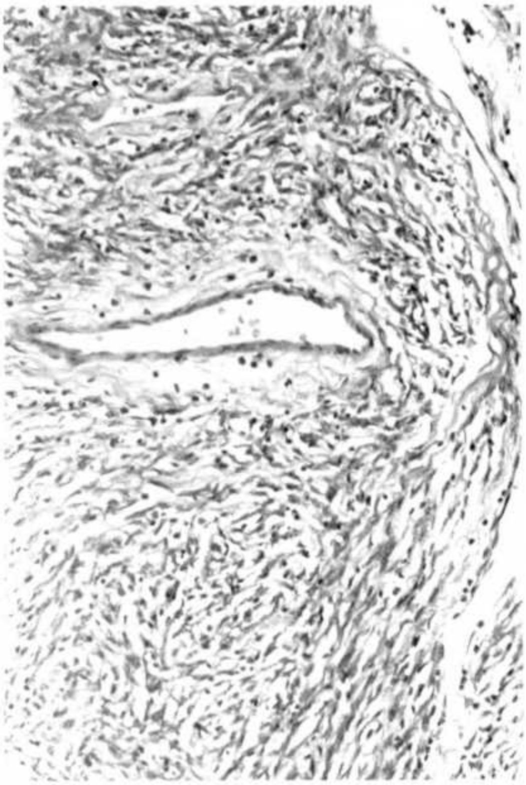


Fig. 3. Photomicrograph showing vascular clefts and intercellular spaces, many of which contain red blood cells. HE. (× 160.)

fibrofatty tissue and required little dissection for complete removal.

The patient made an uneventful recovery from the operation. Over a period of 4 weeks the power in the lower limbs returned to almost normal. The sensory deficit also recovered to a large extent and at the time of his discharge 4 weeks later he was able to walk unaided.

Histological examination revealed a circumscribed cellular nodule measuring 3·8 × 2·5 × 1·5 cm attached at one point to vascular fibrous fatty tissue. An incomplete fibrous capsule partially defined the edge of the nodule. Microscopic examination revealed the predominant cell type to be fibroblastic with vesicular lightly staining nuclei and eosinophilic cytoplasm. In the central region the cells were either plump and ovoid with an ill-defined eosinophilic cytoplasm and irregular reticulin fibres (*Fig.* 1), or spindle-shaped with a compact fasciculated pattern and a regimented arrangement of reticulin fibres. In the peripheral regions the cells were less compact. Only occasional mitotic figures were identified and none had abnormal features. The stroma was highly vascular, particularly at the periphery (*Fig.* 2), with many vascular clefts, and spaces separated the fibroblastic cells. Throughout the tumour red blood cells lay in endothelialized clefts and non-endothelialized intercellular spaces (*Fig.* 3). Occasional vessels were cuffed with sparse accumulations of lymphoid cells. A small amount of collagen was present; no multinucleated cells were identified. Apart from the fat cells at the edge of the nodule no lipid-containing cells were identified to suggest that the tumour had a lipomatous origin and the nodule had no features distinctive of a neurilemoma (no Antoni tissue type A and B and palisading).

Discussion

The term 'nodular fasciitis' is now generally accepted as an apt description of a peculiar lesion which is usually found in subcutaneous or deep fascial planes (Leading Article, 1973). The nodule is generally 1–3 cm in size and has distinctive histological features. It appears as a vascular proliferation of fibroblasts with a patchy lymphocytic infiltration, occasional islands of collagen and occasional giant or multinucleated cells (Price et al., 1961; Mackenzie, 1970). The cellularity of the lesion and the presence of mitotic figures have led to it being confused with a variety of mesodermal tumours and reactive processes, including sarcomas. It usually grows rapidly but it does not metastasize or recur if completely excised (Stout, 1961; Hutter et al., 1962).

Although known to occur in a variety of locations, including the orbit (Font and Zimmerman, 1966), it has not to our knowledge been described as an extradural tumour causing compression of the spinal cord. Analysis of spinal cord tumours in the past (Elsberg, 1941; Kernohan, 1941; Austin, 1961) has listed 'fibromata' as constituting less than 1 per cent of extradural neoplasms. Unfortunately the histology of these fibromata was not described. The origin of nodular fasciitis is still in doubt. Traumatic stimulus has been cited as a possible aetiological factor (Soule, 1962), but in the present case there was no history of trauma to the back. The unusual situation in this case raises the questions of dermal implantation (Manno et al., 1962; James and Lassman, 1972), but a lumbar puncture had not been performed previously. In subcutaneous tissues nodular fasciitis is relatively harmless, but in this case in the confines of the vertebral canal it caused spinal cord compression and paraplegia.

It is important to identify the lesion histologically because, despite its appearance, it is benign (Price et al., 1961; Hutter et al., 1962; Soule, 1962), and in the present case its removal at an early stage has prevented a permanent neurological deficit.

Acknowledgements

The authors wish to thank Professor John Hankinson under whom this patient was admitted, and Professor B. E. Tomlinson for verifying the histology of the tumour.

References

AUSTIN G. (1961) *The Spinal Cord.* Springfield, Ill. Thomas, pp. 104–105.

ELSBERG C. A. (1941) *Surgical Diseases of the Spinal Cord, Membranes and Nerve roots.* New York, Hoeber, p. 49.

FONT R. L. and ZIMMERMAN L. E. (1966) Nodular fasciitis of the eye and adnexa. *Arch. Ophthalmol.* **75**, 475–481.

HUTTER R. V. P., STEWART F. W. and FOOTE F. W. (1962) Fasciitis. *Cancer* **15**, 992–1003.

JAMES C. C. M. and LASSMAN L. P. (1972) *Spinal Dysraphism.* London, Butterworths, pp. 18–24, 57–60.

KERNOHAN J. W. (1941) Tumours of the spinal cord. *Arch. Pathol.* **32**, 843–883.

LEADING ARTICLE (1973) Nodular fasciitis. *Lancet* **1**, 870.

MACKENZIE D. H. (1970) *The Differential Diagnosis of Fibroblastic Disorders*. Oxford, Blackwell, pp. 18–27.

MANNO N. J., KIHLEIN A. and KERNOHAN J. W. (1962) Intraspinal epidermoids. *J. Neurosurg.* **19**, 754–765.

PRICE E. B. jun., SILLIPHANT W. M. and SHUMAN R. (1961) Nodular fasciitis: a clinico-pathological analysis of 65 cases. *Am. J. Clin. Pathol.* **35**, 122–136.

SOULE E. G. (1962) Proliferative (nodular) fasciitis. *Arch. Pathol.* **73**, 437–444.

STOUT A. P. (1961) Pseudosarcomatous fasciitis in children. *Cancer* **14**, 1216–1222.

Errata

British Journal of Surgery, Vol. 62: No. 3: March 1975, p. 195. The legends to *Figs*. 2, 4 and 5 should read as follows:

Fig. 2. Photomicrograph of regenerating liver at 72 hours . . . .

Fig. 4. *Case* 7. Rise in serum bilirubin level after hepatic resection with unconjugated fraction as the main component (type I).

Fig. 5. *Case* 6. Rise in serum bilirubin level after hepatic resection with the conjugated fraction as the main component (type II).

Br. J. Surg. Vol. 62 (1975) 576–580

Peritoneal mesothelioma

P. S. F. CHAN, T. W. BALFOUR, J. B. BOURKE AND P. G. SMITH*

SUMMARY

Two patients with primary peritoneal mesothelioma are reported. They had abdominal symptoms, no symptoms referable to the respiratory system and normal chest X-rays. There was no clinical evidence of impaired respiratory function. One of the patients had a history of brief asbestos exposure over 20 years before diagnosis. The procedure for obtaining compensation is outlined and the protean uses of, and hence possible exposure to, asbestos are noted. In screening programmes consideration should be given to both pulmonary and abdominal symptoms. Laparoscopy may have a part to play in earlier diagnosis of peritoneal mesothelioma.

MESOTHELIOMA is a rare primary tumour of cells which line serosal cavities. It may arise from pleura, peritoneum or pericardium but the typical clinical presentation is as a thoracic or abdominal problem, yet occasionally both may be involved.

Initially, peritoneal mesotheliomas appear as whitish nodules scattered over visceral and parietal peritoneum which later coalesce to form plaques and masses. Characteristically, even with massive tumour growth and in the late stage of the disease, invasion of bowel or adjacent viscera such as liver is limited. As they grow mesotheliomas appear to encase the intraperitoneal contents. Multiple distant deposits do occur but metastasis is typical only to the regional lymph nodes.

Histologically, there is a wide spectrum of appearance varying from a predominantly epithelial pattern on the one hand to an almost pure spindle form on the other; a mixed epithelial and connective tissue pattern is not uncommon. Appearances can vary within a tumour and from patient to patient. The epithelial element may vary from well-differentiated tubules and papillae to solid epithelial formations. Some mesothelioma cells are vacuolated and contain mucin of connective tissue origin.

The criteria for the diagnosis of peritoneal mesothelioma were stated in 1960 by Winslow and Taylor to be: (1) a compatible clinical history, (2) characteristic gross features, (3) characteristic microscopic features and (4) progressive growth of the tumour in the characteristic manner resulting in the death of the patient. Since this report there has been a rising incidence of mesothelioma and this may in part be due to increasing awareness by pathologists (Moertel, 1972).

Patients with peritoneal mesotheliomas typically present with subacute intestinal obstruction and weight loss (Moertel, 1972). The commonest symptom is abdominal pain, while ascites is the commonest physical sign, being present in 90 per cent of cases (Moertel, 1972). A mass is occasionally found and nausea and vomiting are uncommon (Moertel, 1972). The onset of symptoms is insidious but once the diagnosis is made, death usually ensues within a year (Enticknap and Smither, 1964; Newhouse and Thompson, 1965; Smith et al., 1968).

The relationship between asbestos exposure and mesothelioma is well recognized, as is the long latent period of 20–47 years (Wagner et al., 1960; Newhouse and Thompson, 1965; Selikoff et al., 1965).

Two patients with primary peritoneal mesothelioma presented to the Professorial Surgical Unit in Nottingham during a period of just over 1 year and they are reported in detail below.

Case reports

Case 1: A 64-year-old man was admitted as an emergency on 18 February 1973 with a 5-hour history of colicky epigastric pain and vomiting. On examination there was tenderness in the right upper quadrant. A diagnosis of acute cholecystitis was made and he was treated conservatively. His symptoms and signs settled rapidly and he was discharged to outpatient care. A subsequent intravenous cholangiogram showed that the gallbladder contained gallstones. Five weeks later he was readmitted with an exacerbation of his symptoms. Urgent cholecystectomy was performed (27 March) through an upper right paramedian incision. At operation the pancreas was noted to be bulky and there were small white nodules on the omentum and parietal peritoneum which had the appearances of fat necrosis. Histological examination of the gallbladder showed severe chronic cholecystitis. He made a good recovery from operation and was discharged to outpatient care.

Three months after operation he noticed colicky pain around the scar which was aggravated by fatty foods and associated with vomiting. On examination he was found to have a large, irregular, non-tender, hard mass in the right hypochondrium. There was no ascites. He was readmitted on 21 September. He was noticed to have lost 19 kg in weight in the preceding 6 months. Plain abdominal X-ray showed a large soft tissue mass in the right upper quadrant which was displacing the small and large intestine. There were multiple small bowel fluid levels.

Laparotomy (23 September) was performed through the previous incision, and it was difficult to enter the abdominal cavity as in places the peritoneum was between 1 and 2 cm thick, rigid and like marble. There were multiple small white nodules throughout the peritoneal cavity and on the serosal surfaces of the intestine. The small bowel was subacutely obstructed. There was a minimal quantity of peritoneal fluid and some was submitted to bacteriological examination, including culture for tubercle bacilli. Biopsies were taken of serosal nodules and from the peritoneal mass. The diagnosis was uncertain and carcinomatosis was considered the most likely. The patient made a satisfactory recovery from operation.

No acid- and alcohol-fast bacilli were seen on Ziehl-Neelson staining or grown from the peritoneal fluid.

Histology of the biopsies (*Fig.* 1) showed nodular and diffuse infiltration by mesothelioma of a tubulopapillary pattern with clefts and papillae lined by plump epithelial cells with a fibromatous stroma. The nuclei of the epithelial and connective tissue elements were vesicular with prominent red nucleoli.

---

* University Department of Surgery and Department of Pathology, General Hospital, Nottingham.

After the diagnosis of mesothelioma the patient's chest X-rays were reviewed and no evidence of pleural plaques was found. He produced no sputum which could be examined for asbestos bodies. On further close physical examination there was no evidence of finger clubbing or clinical abnormality of his respiratory system. Inquiry into his occupational history revealed that during the Second World War he had fitted asbestos filter pads while assembling respirators. The histology slide of his gallbladder and further sections were reviewed and showed small islands of tissue suggestive of mesothelioma.

The patient was discharged home 3 weeks after operation without specific treatment. He slowly deteriorated and died on 17 February 1974. At autopsy he was emaciated. There were bilateral costal and diaphragmatic hyaline pleural plaques and the lungs contained asbestos bodies. The peritoneal cavity was almost completely obliterated by dense white tumour of up to 2·5 cm thickness on serosal surfaces. In some areas there were discrete nodules but the liver and spleen were encased in tumour. There was no evidence of a primary epithelial neoplasm. The post-mortem findings were in keeping with a primary diffuse peritoneal mesothelioma.

Case 2: A 75-year-old retired policeman with gout was first noticed in 1971 to have a mass in the left iliac fossa. Barium enema examination at this time showed a few diverticula in the descending colon. In May 1972 his general practitioner noticed that he was anaemic with gross ankle oedema and that the mass was still present in his left iliac fossa. He was referred to the Professorial Surgical Unit, Nottingham, for further investigation. The patient then volunteered that he had had intermittent attacks of left iliac fossa pain of about a week's duration since 1964.

Examination at this time showed that he was anaemic (haemoglobin 5 g per cent) with gross ankle and sacral oedema. His liver was enlarged and there was a large, mobile, slightly tender mass in the left iliac fossa. No ascites was detected. A barium enema examination showed an irregular extrinsic mass displacing the medial wall of the descending colon, and excretion urography showed a soft tissue mass indenting the bladder superiorly.

At laparotomy (23 May) there was a minimal quantity of free fluid. Numerous pedunculated tumours arose from the peritoneum and the serosal surfaces of the intestine. The largest was about 8 cm in diameter and was in the left iliac fossa. Multiple biopsies were taken.

Histological examination (*Fig.* 2) showed a solid and epithelial neoplasm with a mucinous and oedematous stroma. The tumour cells had voluminous cytoplasm and some were vacuolated. The features were those of peritoneal mesothelioma.

The patient made an uneventful recovery from operation, apart from an exacerbation of his gout which was rapidly controlled with phenylbutazone, and he was discharged home. His chest X-rays were reviewed and no evidence of pleural plaques was detected. Between September 1972 and July 1973 he was admitted to hospital three times for blood transfusion and twice with subacute intestinal obstruction which responded to conservative management. He died at home in July 1973 and a post-mortem examination was not performed.

After death, his family was interviewed and there did not appear to be any history of domestic or industrial exposure to asbestos.

Discussion

Much greater quantities of asbestos were used during and immediately after the Second World War than ever before. Since the recognition of the relationship between asbestos exposure and the development of mesothelioma (Enticknap and Smither, 1964; Newhouse and Thompson, 1965; Smith et al., 1968) Selikoff et al. (1965) have suggested that the occurrence of these neoplasms has and will continue to increase.

The 2 patients reported here contrast in their clinical presentation. *Case* 1 showed no symptoms typically associated with mesothelioma (Moertel, 1972) until after cholecystectomy when the overlooked intra-abdominal neoplasm grew rapidly and formed a massive tumour within a few months. Lazarus et al. (1971) reported a similar rapid development of an 8-cm mesotheliomatous mass in the left upper quadrant of the abdomen 6 months after laparotomy. *Case* 2 presented with insidious symptoms of several years' duration, and anaemia ultimately precipitated his full investigation. On clinical examination both patients had abdominal masses and neither had ascites. Reports in the literature (Winslow and Taylor, 1960; Enticknap and Smither, 1964; Smith et al., 1968; Moertel, 1972) have noted that ascites is common and masses are rarely found. It thus seems that awareness by surgeon and pathologist alike may be a major factor in making the diagnosis.

Abnormal chest X-rays are frequently found in asbestos workers who subsequently develop peritoneal mesothelioma (Mann et al., 1966; Borow et al., 1967; Smith et al., 1968; Roberts and Irvine, 1970). Of the 2 patients reported here, neither showed chest radiological abnormality in spite of *Case* 1 having pleural and diaphragmatic plaques at autopsy and a history of brief asbestos exposure.

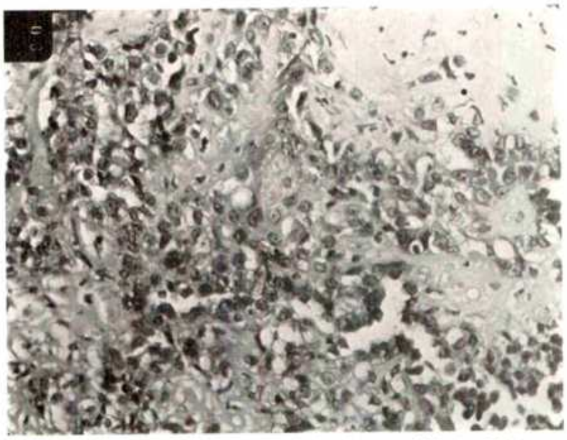


Fig. 1. *Case* 1. Mesothelioma of mixed type. HE. (× 220.)

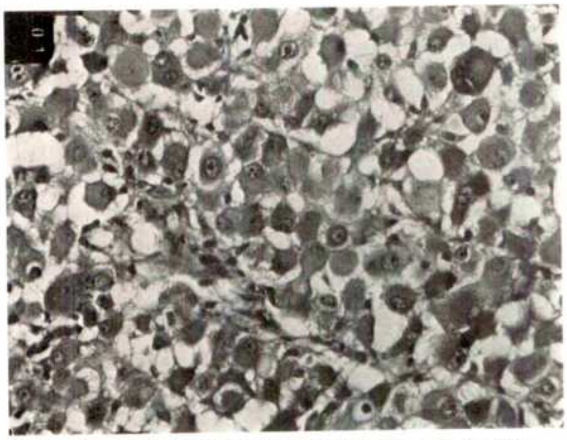


Fig. 2. *Case* 2. Epithelial type mesothelioma. HE. (× 250.)

Special laboratory investigations are unhelpful in diagnosis, and radiology offers little specific aid apart from excluding gross pleural involvement or showing small flakes of calcification in diaphragmatic plaques (Borow et al., 1967; Moertel, 1972). Extrinsic pressure or encasement of part of the gastro-intestinal tract by tumour may be seen on barium investigation but the findings are non-specific (Lazarus et al., 1971).

On histological examination vacuolated epithelial elements are seen, but their contents do not stain like epithelial mucin. However, the contents of the vacuoles may be demonstrated with metachromatic stains such as thionin, and the major substance present is hyaluronic acid (Winslow and Taylor, 1960). Metachromatic staining within the tumour and its removal by hyaluronidase is thus strong evidence for the diagnosis of mesothelioma (Winslow and Taylor, 1960; McCaughy, 1965). Kannerstein et al. (1973) have noted that histochemical methods will not resolve all the problems in the histological diagnosis of mesothelioma but they do have a supporting role. However, it is in patients where diagnosis is difficult that the possibility of a positive reaction to histochemical staining is least likely. Ascitic and pleural fluid should be routinely screened for hyaluronic acid, as this may be found with mesothelioma (Harrington et al., 1963). However, Boersma et al. (1973) have shown that the presence of hyaluronic acid in tissue fluid is not specific to mesothelioma and may occur with other cancers. They concluded that the presence of hyaluronic acid in effusions or tissue biopsies should be one criterion for the diagnosis of mesothelioma which was useful when histology or pathology was equivocal. It should be remembered that Spicer et al. (1967) have referred to the lack of identity in histochemical and biochemical characterization of the mucopolysaccharides. Butler and Berry (1973) have reported that malignant mesothelioma may be diagnosed by exfoliative cytology. This depends on the recognition of cells which show the cytoplasmic differentiation of mesothelial cells and have nuclei with the usual criteria for malignancy. In patients with peritoneal mesothelioma this technique may be of value as the commonest physical sign is ascites (Moertel, 1972). Peritoneal fluid obtained at laparotomy should also be examined by this technique. The specimens should be divided into two and part placed in a dry sterile container and the remainder into a citrated bottle for making suitable cytological preparations.

Laparoscopy, biopsy and exfoliative cytology may have a place in early diagnosis if suspicion is high. However, this may only occur if an appropriate industrial history of asbestos exposure or contact is obtained. This may not always be possible, for only one of our patients had such a history. Biopsy specimens from suspicious tumours should also be taken into alcohol fixative so as to preserve the water-soluble hyaluronic acid which forms a large part of the mucin produced by a mesothelioma. If specimens are placed in formalin fixative hyaluronic acid may be lost from the tissue and cytoplasmic vacuoles may appear empty (Harries et al., 1973).

Treatment is unsatisfactory, as is shown by the survival from diagnosis to death being typically less than 1 year (Enticknap and Smither, 1964; Newhouse and Thompson, 1965; Borow et al., 1967; Smith et al., 1968; Moertel, 1972). However, it should be noted that *Case* 2, who did not have a history of industrial exposure, survived for 14 months. Systemic, intrapleural and intraperitoneal cytotoxic therapy and radiotherapy have all been used with little success (Moertel, 1972). This may in part be due to the lesion presenting at an advanced stage when a large tumour mass is present. It is tempting to speculate what might have been achieved in *Case* 1 if cytotoxic therapy had been prescribed if the diagnosis had been made after cholecystectomy as at that stage the tumour mass was small.

At present the relatives of a patient with mesothelioma become eligible for compensation if asbestos or asbestos bodies are found in the lungs with or without pulmonary fibrosis. Death is reported to HM Coroner who may order an autopsy and also hold an inquest. The findings are reported to the Pneumoconiosis Panel and compensation may be awarded. At autopsy it is important to exclude a gastro-intestinal neoplasm. Elmes and Wade (1965), Selikoff et al. (1968), McDonald et al. (1970) and Selikoff et al. (1973) have reported excess mortality from gastric, colonic and rectal carcinoma in groups of asbestos workers. However, Newhouse (1973) is of the opinion that the evidence for this increased risk is inconclusive.

In patients dying from mesothelioma without an appropriate industrial history HM Coroner should still be informed so that an autopsy can be performed, as only in this way may the asbestos be identified and compensation obtained for the relatives.

It seems that asbestos will continue to be widely used commercially as this mineral breaks down on crushing into fibres which have great tensile strength and excellent thermal and electrical insulating properties. Asbestos fibre can be spun and used to make safety curtains and clothes. It may be used to form asbestos cement for insulation or protection from corrosion by substances such as sea water and acid, or it can be added to plastics to produce insulating materials. In this country exposure to asbestos is greatest in those employed in processing asbestos, and primary manufacturers take extensive safety measures (*Asbestos and Your Health*, *Working with Asbestos*; Howard, 1974; *Health and Safety at Work*, 1974). There is also much casual exposure to asbestos, such as when asbestos building board is sawn up where typically no precautions are taken and the worker is probably unaware of any health hazard (Martin, 1970). The building board itself is not the hazard, but asbestos is released into the atmosphere for inhalation by the worker when the sheeting is sawn up (Martin, 1970; *Health and Safety at Work*, 1974). The abandon with which asbestos lagging is ripped from pipes as buildings are refurbished contrasts with the strict care taken in HM Dockyards when asbestos lagging is removed and replaced (Elmes, 1966; Harries, 1968; *Health and Safety at Work*, 1974).

Persons employed by primary asbestos users have serial lung function tests and chest X-rays performed to assess the development and prognosis of asbestosis (Harries, 1968; Mackenzie, 1971). Those with repeated random exposure to asbestos, such as building workers, are typically not screened for the development of asbestosis, and ongoing medical surveillance would probably be impossible because the mobility of the labour force is high. In addition, the latent period for the development of mesothelioma is typically between 20 and 35 years (Enticknap and Smither, 1964; Newhouse and Thompson, 1965; Smith et al., 1968). This further emphasizes the importance of taking an adequate and detailed industrial history.

The 2 patients reported here had only abdominal symptoms, normal chest radiology and no routine clinical evidence of impaired respiratory function, although sophisticated studies were not performed. In screening asbestos workers consideration should be given to both pulmonary and abdominal symptoms. It may be that laparoscopy in appropriate patients could play an important part in earlier diagnosis and this may make the lesion amenable to therapy and thus improve the present dismal prognosis.

Acknowledgement

We wish to thank Professor J. D. Hardcastle for allowing us to report his patients.

References

Asbestos and Your Health, Leaflet produced by the Asbestos Information Committee, 2 Old Burlington Street, London W1X 2LH.

BOERSMA A. A., DEGAND P. and HAVEZ R. (1973) Diffuse mesothelioma: biochemical stages in the diagnosis detection and measurement of hyaluronic acid in the pleural fluid. In: BOGOVSKI P., GILSON J. C., TIMBRELL V. and WAGNER J. C. (ed.) *Biological Effects of Asbestos, Proceedings of a Working Conference held at the International Agency for Research on Cancer, Lyon, France. 2–6 October*, 1972, pp. 62–64.

BOROW M., CONSTON A., LIVORNESE L. L. and SCHALET N. (1967) Mesothelioma and its association with asbestosis. *JAMA* **201**, 587–591.

BUTLER E. B. and BERRY A. V. (1973) Diffuse mesotheliomas: diagnostic criteria using exfoliative cytology. In: BOGOVSKI P., GILSON J. C., TIMBRELL V. and WAGNER J. C. (ed.) *Biological Effects of Asbestos, Proceedings of a Working Conference held at the International Agency for Research on Cancer, Lyon, France. 2–6 October*, 1972, pp. 68–73.

ELMES P. C. (1966) The epidemiology and clinical features of asbestosis and related diseases. *Postgrad. Med. J.* **42**, 623–629.

ELMES P. C. and WADE O. L. (1965) Relation between exposure to asbestos and pleural malignancy in Belfast. *Ann. NY Acad. Sci.* **132**, 549–557.

ENTICKNAP J. B. and SMITHER W. J. (1964) Peritoneal tumours in asbestosis. *Br. J. Ind. Med.* **21**, 20–31.

HAMMOND E. C., SELIKOFF I. M. and CHURG J. (1965) Neoplasia among insulation workers in the United States with special reference to intra-abdominal neoplasia. *Ann. NY Acad. Sci.* **132**, 519–525.

HARRIES P. G. (1968) Asbestos hazards in naval dockyards. *Ann. Occup. Hyg.* **11**, 135–142.

HARRIES P. G., JONES J. S. P., SKIDMORE J. W. and SMITH P. G. (1973) Symposium on diseases associated with asbestos dust exposure. *Bull. Int. Acad. Pathol.* **14**, 9–7.

HARRINGTON J. S., WAGNES J. C. and SMITH M. (1963) The detection of hyaluronic acid in pleural fluids of cases with diffuse pleural mesotheliomas. *Br. J. Exp. Pathol.* **44**, 81–87.

Health and Safety at Work. Booklet 44. *Asbestos: Health Precautions in Industry* (1974). London, HMSO.

HOWARD W. P. (1974) Health risks in industry (Letter to the Editor). *The Times*, Saturday, 12 May 1974.

KANNERSTEIN M., CHURG J. and MAGNER D. (1973) Histochemical studies in the diagnosis of mesothelioma. In: BOGOVSKI P., GILSON J. C., TIMBRELL V. and WAGNER J. C. (ed.) *Biological Effects of Asbestos, Proceedings of a Working Conference held at the International Agency for Research on Cancer, Lyon, France. 2–6 October*, 1972, pp. 62–64.

LAZARUS H., WIDRICH W. C. and ROBBINS A. H. (1971) Peritoneal mesothelioma with roentgenographic findings. *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **113**, 171–173.

MCCAUGHY W. T. E. (1965) Criteria for diagnosis of diffuse mesothelial tumours. *Ann. NY Acad. Sci.* **132**, 603–613.

MCDONALD A. D., HARPER A., EL-ATTAR O. A. and MCDONALD J. C. (1970) Epidemiology of primary malignant mesothelial tumours in Canada. *Cancer* **26**, 914–919.

MACKENZIE F. A. F. (1971) The radiological investigation of the early manifestations of exposure to asbestos dust. *Proc. R. Soc. Med.* **64**, 834–837.

MANN R. H., GROSH J. L. and O'DONNELL W. M. (1966) Mesothelioma associated with asbestosis. *Cancer* **19**, 521–526.

MARTIN A. E. (1970) Asbestos in the environment: possible hazards to the general population. *Health Trends* **2**, 10–21.

MOERTEL C. G. (1972) Peritoneal mesothelioma. *Gastroenterology* **63**, 346–350.

NEWHOUSE M. L. (1973) Cancer among workers in the asbestos textile industry. In: BOGOVSKI P., GILSON J. C., TIMBRELL V. and WAGNER J. C. (ed.) *Biological Effects of Asbestos, Proceedings of a Working Conference held at the International Agency for Research on Cancer, Lyon, France. 2–6 October*, 1972, pp. 203–208.

NEWHOUSE M. L. and THOMPSON H. (1965) Mesothelioma of pleura and peritoneum following exposure to asbestos in the London area. *Br. J. Ind. Med.* **22**, 261–169.

ROBERTS G. H. and IRVINE R. W. (1970) Peritoneal mesothelioma. *Br. J. Surg.* **57**, 645–650.

SELIKOFF I. J., CHURG J. and HAMMOND E. C. (1965) Relation between exposure to asbestos and mesothelioma. *New Engl. J. Med.* **272**, 560–565.

SELIKOFF I. J., HAMMOND E. C. and CHURG J. (1968) Asbestos exposure, smoking and neoplasia. *JAMA* **188**, 22–26.

SELIKOFF I. J., HAMMOND E. C. and SEIDMAN H. (1973) Cancer risk in insulation workers in the United States. In: BOGOVSKI P., GILSON J. C., TIMBRELL V. and WAGNER J. C. (ed.) *Biological Effects of Asbestos, Proceedings of a Working Conference held at the International Agency for Research on Cancer, Lyon, France. 2–6 October*, 1972, pp. 209–216.

SMITH P. G., HIGGINS P. MCR. and PARK W. D. (1968) Peritoneal mesothelioma presenting surgically. *Br. J. Surg.* **55**, 681–684.

SPICER S. S., HORN R. G. and LEPPI T. J. (1967) Histochemistry of connective tissue mucopolysaccharides. In: WAGNER B. M. and SMITH D. E. (ed.) *The Connective Tissue.* Baltimore, Williams & Wilkins, pp. 251–303.

WAGNER J. C., SLEGGS C. A. and MARCHAND P. (1960) Diffuse pleural mesothelioma and asbestos exposure in the Northwestern Cape Province. *Br. J. Ind. Med.* **17**, 260–271.

WINSLOW D. J. and TAYLOR H. B. (1960) Malignant peritoneal mesotheliomas. *Cancer* **13**, 127–136.

Working with Asbestos, Ministry of Defence (Navy) Publication N/L 90/66.

Br. J. Surg. Vol. 62 (1975) 581–583

The negative cholecystogram in gallbladder disease

D. R. K. REID AND I. M. ROGERS*

SUMMARY

Seventeen cases of radiologically negative gallbladder disease are presented. In all it was possible to explain the symptoms on the basis of the 'disappearing stone' hypothesis. It is suggested that cholecystectomy should be advised in such patients provided that the symptoms are sufficiently characteristic and sufficiently severe.

THERE is a general assumption that the diagnosis of gallbladder disease should, in all instances, rest on the cholecystogram. It is the purpose of this paper to advance the proposition that biliary colic, implying gallstones, occurs with a clinically significant frequency when the cholecystogram is normal.

It is our impression that most surgeons (and practically all physicians) would demand positive X-rays before advising surgery, whereas we believe that the clinician should be prepared to advise cholecystectomy despite a negative report if he is convinced that the symptoms are sufficiently typical, sufficiently severe and sufficiently persistent.

Patients

Seventeen patients are presented. They are characterized by typical, severe and recurrent biliary colic, negative cholecystography on at least one occasion and complete relief of their pain after cholecystectomy.

Incidence

Most of these patients have occurred in the practice of one of us (D. R. K. R.) over a period of 10 years, during which 40–50 cholecystectomies have been performed annually. They therefore represent a small (approximately 3 per cent) but none the less interesting and important group.

Age and Sex

There were 2 males and 15 females with ages ranging from 21 to 70 years (average 43 years).

Symptoms

The *duration* of symptoms ranged from 6 months to 25 years with an average duration of 7·5 years. In every case there was a period of observation lasting at least some months before a final diagnosis was made and surgery advised.

Pain was the main symptom in all the cases and was a prerequisite for inclusion in the series. The pain was of a typical nature and distribution with severe and recurrent attacks which lasted from several hours to several days. Patients in whom a psychosomatic disorder or emotional instability was suspected were not included.

Radiographic findings

On at least one occasion a normal cholecystogram had been reported in each patient. The cholecystogram had been repeated several times in 6 patients, and in 3 instances a normal intravenous cholangiogram had been obtained. One patient had one normal cholecystogram and one normal intravenous cholangiogram (*Table* 1).

The cholecystogram was reported as abnormal on one occasion in 4 patients. In 2 patients normal findings on cholecystography became abnormal (radiolucent filling defects) over periods of 5 and 11 years respectively, while the symptoms remained the same. The remaining 2 patients had an abnormal cholecystogram initially but normal findings were reported after periods of 3 and 9 months respectively (*Table* 1).

Jaundice

Transitory jaundice had occurred in 5 patients, and in 1 six times. Two of these patients had a few cholesterol stones in the gallbladder, 1 had biliary mud and 2 had no stones at operation.

Three patients developed dark urine and pale stools during or soon after an attack of typical pain. This clinical state has been described as 'subclinical' jaundice, and it is interesting to note that it occurred both in patients with and without stones at operation (*Table* 1).

Stones

There are few differences between the 9 patients with stones and the 8 patients without stones at operation (*Table II*). The frequency of jaundice and the incidence of cholecystitis are nearly the same. Both groups were totally relieved of their attacks of pain by cholecystectomy, and the postoperative follow-up period is similar.

In 3 patients the stones were of mixed type, and in 2 of these the cholecystogram findings changed from normal to abnormal over periods of 5 and 11 years respectively. In 1 case biliary mud rather than stones was found, and in the remaining 6 the stones were small and yellow, measured 2–3 mm in diameter and numbered no more than 2 or 3 in any one case. They were obviously of cholesterol composition. The stones were usually within the gallbladder, but in one instance a small stone was removed from the cystic duct. Duct stones were not found despite 4 duct explorations.

---

* Glasgow Royal Infirmary.

Table I: DETAILS OF THE PRESENT SERIES

Group	Patient	Age	Duration of pain	Jaundice: Clinical	Jaundice: Sub-clinical	X-ray findings	Stones	Histo-logical findings	Relief from pain	Follow-up	CCK
I	Mr J. B.	52	25 yr	+*	—	−ve ×3	+	+	+	10 yr	—
	Mrs M. E.	24	2 yr	+	—	−ve ×1	—	+	+	2 yr	—
	Mrs R. D.	47	4 yr	+	—	−ve ×1	+	+	+	4 yr	—
	Mrs S. H.	23	10 mth	+	—	−ve ×2	+	+	+	7 mth	Equivocal
II	Mrs G. M.	31	5 yr	—	—	−ve ×1	+	+	+	3 yr	—
	Mrs A. M.	43	10 yr	—	—	−ve ×2	+	+	+	8 yr	—
	Mrs M. W.	70	20 yr	—	—	−ve ×2	+	+	+	1 yr	—
	Mrs M. C.	48	1 yr	—	+	−ve ×1	+	+	+	1 yr	—
III	Mrs D. K.	46	25 yr	—	—	−ve ×1	—	+	+	5 yr	—
	Mrs R. G.	48	3 yr	—	—	−ve ×1	—	+	+	7 yr	—
	Mrs A. D.	28	8 mth	—	+	−ve ×2	—	+	+	9 mth	Positive
IV	Mrs B. S.	21	6 mth	—	—	−ve ×1	—	—	+	6 mth	—
	Miss M. M.	54	3 yr	—	+	−ve ×2	—	—	+	1 yr	Positive
V	Mr D. M.	54	5 yr	—	—	−ve→+ve	+	+	+	1½ yr	—
	Mrs J. D.	54	12 yr	—	—	−ve→+ve	+	+	+	6 mth	—
VI	Mrs M.	25	2 yr	+	—	+ve→−ve	—	+	+	6 mth	—
	Mrs Mac.	50	2 yr	—	—	+be→−ve	—	+	+	6 mth	—

* This patient had six attacks of jaundice.
CCK, Cholecystokinin test. Result, when performed, shown.
−ve, Negative; +ve, positive.

Table II: PRESENCE OR ABSENCE OF STONES AT OPERATION

	Stones	No stones
Number of cases	9	8
Clinical or subclinical jaundice	4	3
Cholecystitis on histological examination	9	6
Follow-up (yr)	3·0	2·15

Pathological findings

The gross appearance of the stone-containing gallbladder at operation was usually within normal limits. Histological appearances varied from minimal to mild cholecystitis. All the patients with stones showed inflammatory change and all but 2 of the patients without stones at operation showed similar changes (*Table II*).

Follow-up

Freedom from attacks of pain was immediate and complete in all the patients over periods ranging from 6 months to 10 years (average 2 years 9 months). Most patients were eating freely and taking fat. Few clinicians would dispute that when a stone-containing gallbladder is removed from a patient suffering from attacks of biliary colic the attacks of pain are likely to cease. What is of interest in our series is that patients without stones at operation are similarly relieved of pain over a comparable follow-up period (*Table II*).

Discussion

Before operation the whole group was clinically indistinguishable, but subsequently they may be divided into those with and without stones in the gallbladder. In the former the calculi were of cholesterol and few in number, suggesting that the patients suffered from lithogenic bile (Small, 1968). In the latter the frequency of jaundice or subclinical jaundice and the postoperative freedom from pain make for the belief that stones previously present had migrated down the biliary tree and been expelled (Addleman, 1962; Gray, 1974).

Both situations are supported by evidence from other reports. Normal cholecystography has been associated with the finding of stones at operation (Large, 1968), and in patients with typical biliary colic the removal of an acalculous gallbladder has relieved pain (Mackey, 1934; Valberg et al., 1971; Gunn, 1973). In the acalculous patients both biochemical evidence of obstructive jaundice and structural abnormalities of the gallbladder have been common.

The significance of the histological appearances of cholecystitis is uncertain. When present it might suggest that stones have previously been in the gallbladder; when absent metabolically formed stones as former residents are not excluded.

We have based our diagnosis and also our hypothesis that this clinical group of patients is composed of those who have stones in the biliary tree which come and go entirely on clinical grounds. Provocation of an attack of pain with cholecystokinin is said to be of help in establishing a diagnosis of pain of biliary origin (Cozzolino et al., 1963; Valberg et al., 1971). We have used this test in some of our patients and have reported upon it previously (Reid et al., 1975). However, we feel that the clinical evidence is such that the clinician should be willing to make a diagnosis of gallbladder origin for pain and to recommend cholecystectomy in spite of negative X-rays when there is typical biliary colic, when all other causes have been excluded and the symptoms are severe. His decision would be supported by clinical or biochemical evidence of obstructive jaundice. In all instances an adequate period of observation should be allowed extending to months or, as with some individuals in our series, to years. Only in this way will the clinician become convinced of the need for operation.

Acknowledgements

We would like to thank Mr Tom Menzies, Consultant Surgeon, Glasgow Royal Infirmary, for permission to include one of his patients in our series and also Mr John Hutchison for permission to report on 2 patients under his care.

References

ADDLEMAN W. (1962) Can gall-stones disappear spontaneously? *Am. J. Gastroenterol.* **37**, 656–659.

COZZOLINO H. J., GOLDSTEIN F., GREENING R. R. and WIRTS C. W. (1963) The cystic duct syndrome. *JAMA* **185**, 920–924.

GRAY R. (1974) Disappearing gall-stones—a report of two cases. *Br. J. Surg.* **61**, 101–103.

GUNN A., KEDDIE N. C. and FOX H. (1973) Acalculous gall-bladder disease. *Br. J. Surg.* **60**, 213–215.

LARGE A. M. (1968) Gall-bladder disease with X-ray films that appear normal. *Arch. Surg.* **96**, 855–857.

MACKEY W. A. (1934) Cholecystitis without stone. *Br. J. Surg.* **22**, 274–295.

REID D. R. K., ROGERS I. M. and CALDER J. F. (1975). The cholecystokinin test: an assessment. *Br. J. Surg.* **62**, 317–319.

SMALL D. M. (1968) Gallstones. *New Engl. J. Med.* **279**, 588–593.

VALBERG L. S., JABBARI M., KERR J. W., CURTIS A. C., RAMCHAND S. and PRENTICE R. S. A. (1971) Biliary pain in young women in the absence of gall-stones. *Gastroenterol.* **60**, 1020–1026.

Br. J. Surg. Vol. 62 (1975) 584–588

Reviews and notices of books

Chirurgie

P. A. A. Klok. 243×167 mm. Pp. 474+xi. Illustrated. 1974. Amsterdam: De Erven Bohn BV. No price given.

A PATIENT referred to a specialist will often ask the opinion of his general practitioner on suggested surgical treatment. This book, written in Dutch, aims to bring the general practitioner up to date on the recent developments in the surgical field. The author gives a survey of general surgery including traumatology, orthopaedics, urology and cardiovascular surgery. In some ways the book is comparable to Taylor and Cotton's *Short Textbook of Surgery*, although less attention is given to the pathophysiological basis of diseases. It combines the advantages and disadvantages of being written by one author. On the other hand, a comparatively complete survey of the Dutch surgical literature of the past 10 years is obtained.

H. MULLER

Vascular Surgery. Volume I. Peripheral Arterial Diseases

John J. Cranley, Cincinnati. 254×200 mm. Pp. 282+xvi. Illustrated. 1972. London: Harper & Row. £11.

THE author is to be complimented on the lucid format and easily readable style of this interesting and informative book. Whilst written on the basis of personal experience due recognition is readily accorded to the work of others, and appropriate references are provided at the end of each chapter.

The subject matter is well chosen and comprehensively covered, but the commentary is concise and to the point with a clear exposition of essential principles. Clinical common sense coupled with sound practical advice permeate the work and experienced surgeons will readily recognize familiar problems. This sense of empathy adds to the enjoyment of the book and the counsel proffered may hopefully dissuade younger surgeons in training from making similar mistakes. The standard of presentation is uniformly high throughout and all the chapters can be perused with profit, those on aneurysmal disease being especially good.

All these features together with the clarity of the illustrations combined with good photography and excellent angiographic reproductions have produced a book which it is a pleasure to recommend to all surgeons with an interest in this subject.

G. SLANEY

The Liver and Its Diseases

Fenton Schaffner, Sheila Sherlock, and Carroll M. Leevy. 180×250 mm. Pp. 353+xi, with 159 illustrations. 1974. Stuttgart: Georg Thieme Verlag. DM.129.

THREE invited contributors have compiled this book discussing their own specialized interest in liver disease. Not one of them is a surgeon so the emphasis is on the medical and biochemical aspects of the damaged liver. The book is dedicated to Hans Popper on his seventieth birthday and begins with an appropriate citation of Popper's work followed by a short so-called 'philosophic statement' on hepatology in 1974.

There are chapters on the electron microscopic ultrastructure of the liver, the liver's handling of drugs, protein synthesis, bilirubin metabolism, the virology of hepatitis and liver biopsy.

In the middle of the book is a short, rather interesting, account of the history of treatment of liver disease called inappropriately 'Liver Therapy' since it does not discuss any treatment with the whole liver or its extracts. There are some fine illustrations of some of the early hepatologists, including Francis Glisson, and a remarkable picture of the so-called 'corset liver' showing the anatomical distortion produced by the fashion of 'wasp waists'. The book then returns to biochemistry, this time of the hepatitis B antigen. There are further chapters on hepatitis and hepatotoxicity due to drugs, including alcohol. The hepatorenal syndrome is treated rather superficially. There is quite an interesting article on the management of portal hypertension, but since it is compiled by a physician the surgical difficulties encountered in operating on patients with liver failure, coagulation defects and gross portal hypertension have not been given sufficient emphasis. Prophylactic portacaval shunts are condemned, and it is pointed out that the survival of patients with a therapeutic shunt is little improved compared with that of untreated patients. The author does, however, come out in favour for certain therapeutic shunts. Cancer of the liver gets half as much space as Wilson's disease.

The book will no doubt be of interest to physicians treating liver disease but has very little of value for the practising surgeon. When the physicians have failed and the patient is dying of liver disease, a new liver would seem to be a logical form of treatment, yet liver transplantation does not even appear in the index!

R. Y. CALNE

Hair Transplant Surgery

O'Tar T. Norwood, Oklahoma. 255×170 mm. Pp. 108+xiii, with 69 illustrations. 1973. Springfield, Ill.: Charles C. Thomas. $10.50.

JUDGING by the present spate of inquiries about hair transplants, this book will interest dermatologists and plastic surgeons, whether or not they actually intend to carry out hair transplant procedures. However, the author warns the reader that the instruction in the book is insufficient for him to practise hair transplants without either joining a formal training programme or observing the procedure.

The monograph commences with a practical (if rather complex) classification of male pattern baldness. It covers comprehensively the selection of cases, the technique of hair transplant surgery and the complications. There is a discussion on the best size of graft to use, and the results of a questionnaire sent to those practising hair transplants about their technique and complications are included. There is a short final chapter reviewing the research in the use of hair-bearing homographs.

The use of the author's technique in alopecias other than male pattern baldness is briefly mentioned. More information would have been welcome here but perhaps the brevity reflects the relative lack of success.

The book is well illustrated, demonstrating the technique of hair transplants in detail, and there is a colour section containing 64 pictures of patients before and after treatment.

B. D. G. MORGAN

Surgical Aspects of Haemodialysis

P. R. F. Bell, Leicester, and K. C. Calman, Glasgow. 234×153 mm. Pp. 130+xii. Illustrated. 1974. Edinburgh: Churchill Livingstone. £4·50.

THIS book has been carefully thought out and is written in a style which is clear and easy to read. Points such as the preparation of the patient and anaesthetic techniques have not been forgotten, and the descriptions of surgical procedures are clear enough to be followed readily. The line drawings are simple and informative, though one is left with a wish for more coloured plates. There is a detailed bibliography related to each procedure which in itself makes a valuable contribution.

The authors have not entered into any discussion on the prevention of complications and how they affect the responsibility of the physician in relation to these surgical aspects of hemodialysis.

The volume is compact and concise. It will be invaluable to the student in this field and is likely to be regarded as a most useful practical manual by those gaining experience of practical work in this speciality.

ROSEMARIE BAILLOD

Atlas of Vascular Surgery

Robert R. Linton, Boston. 310 × 240 mm. Pp. 504 + xviii. Illustrated. 1973. London: W. B. Saunders Company. £27·65.

THIS expensive and lavishly produced work based on the personal experience of an internationally acknowledged master vascular surgeon disappointingly fails to measure up to expectation.

Both the introduction and part 1, dealing with diseases of veins, are strikingly devoid of modern methods of assessment. The section on thrombo-embolic disease is especially poor in this respect, for the radiofibrinogen uptake test, Doppler scanning and the prophylactic effect of subcutaneous heparin, to mention but a few, are not even mentioned. The views expressed regarding management and the vigorous advocacy of venous interruption will certainly not find general acceptance among surgeons in this country.

By comparison, the sections in part 2, dealing with arterial disease, are of high standard, containing an abundance of practical points, invaluable to the tyro and inducing a sense of *déjà-vu* in the experienced. The portions on aortic aneurysmal disease are easily the best in the entire work though even here minor points of contention exist; for example, few surgeons now advocate complete removal of the aneurysm. The management of aorto-iliac occlusive disease is very adequately dealt with, but many would not share the author's opinion that aortography is seldom indicated, or his strong condemnation of the bypass principle without division of the aorta because of the risk of graft thrombosis.

The saphenous vein bypass for femoropopliteal disease is well described, though some aspects of technique are at variance with those generally accepted. Few British surgeons would agree that total removal of a popliteal aneurysm and its accompanying vein is either wise or necessary, or that superficial femoral vein ligation at the groin should be performed as a preliminary to low thigh amputation to prevent subsequent pulmonary embolism.

In the section on cerebrovascular insufficiency, disease of the brachiocephalic trunks is dismissed on one page and the value of bypass procedures for multiple lesions and in poor risk patients is not discussed. Carotid endarterectomy is well described but techniques for vertebral artery insufficiency are not mentioned.

It is regrettable that some portions of this atlas are disappointing because the remainder contains much worthwhile practical advice, especially for young surgeons in training. The standard of the colour illustrations is high but their number could be reduced without detriment. The corresponding reduction in cost might be an important consideration in a book currently priced at £27·65.

G. SLANEY

Roentgen Examinations in Acute Abdominal Diseases

J. Friemann-Dahl, Oslo. Third edition. 230 × 150 mm. Pp. 617 + xiv, with 432 illustrations. 1974. Springfield, Ill.: Charles C. Thomas. $29.50.

THE third edition of this book which now appears 14 years after the previous one carries the same stamp of authority that characterized the original work. So much of our knowledge of the radiological interpretation of the acute abdomen has stemmed from this author that it is perhaps hard to realize that much of the information that is now accepted as commonplace was included as original observations in the first edition.

The hospital where the author practised was orginally responsible for much of our knowledge of plain radiography and, more recently, of abdominal aortography, and it is gratifying to see in this new edition the appropriate attention being given to this newer method of examination. Perhaps in the United Kingdom the value and potentiality of arteriography in acute abdominal vascular conditions and in closed abdominal trauma are not yet fully realized.

Throughout this book the superb quality of the radiographs stands out and there is no doubt that many of the errors of interpretation that occur are the direct results of attempts to interpret films of inadequate quality. Perhaps some of the illustrations where the original blocks have been retained show some loss of their original crispness.

In acute abdominal emergencies it is unfortunate that expert radiological assistance which always should be available is often not consulted, as although the dramatic signs of perforation and obstruction are usually easily recognized the finer and less obvious features which may be vital are not appreciated. This book presents an authoritative and detailed study of these features which would well repay serious study.

A few statements that have been carried on from earlier editions such as 'the importance of fluoroscopy in chest conditions' could well be edited from future editions, and the too frequently occurring spelling errors unreasonably detract from this excellent book.

Besides the value of this authoritative book to radiologists, it should be readily available for reference in any emergency department where radiological investigations of the acute abdomen are made.

The publishers of the book maintain an excellence and quality in keeping with their other productions for which they have gained universal acclaim.

ERIC SAMUEL

Surgical Technology. Basis for Clinical Practice

Mary Louise Hoeller, St Louis, Missouri. Third edition. 245 × 170 mm. Pp. 386 + xii, with 295 illustrations. 1974. London: Henry Kimpton. £5·20.

BRITISH readers may be puzzled by the title. The previous two editions were entitled *The Operating Room Technician*, which is more explicit to us. The book describes modern American views on the organization, training and practice in the operating theatre. The changed title is intended to reflect the response of theatre staff to technical advances in surgical procedures.

To the surgeon the book presents a hotch-potch of anatomy, operative detail, theatre equipment, anaesthetic and radiological techniques, sterile trolley layouts, legal requirements, patient handling and theatre organization. However, at a time of readjustment within the Health Service, when operating theatre resources are overstretched, progressive American views on the total running of theatres is of great interest to those involved in planning and administration. This book offers a stimulating view of the theatre to those working full-time as nurses and technicians. To the surgeon it displays the careful organization and training behind the efficient scrub-nurse handing him instruments.

R. M. KIRK

Cardiovascular Applications of Ultrasound

Edited Robert S. Reneman. 240 × 165 mm. Pp. 462 + xv. Illustrated. 1974. New York: American Elsevier Publishing Company. $28.90.

THIS book contains the proceedings of an international symposium held in Belgium in May 1973. As the editor points out, the importance of ultrasound in cardiology, cardiovascular physiology and pharmacology is growing fast, and the contributors to this book include a number of the most active investigators in the field.

In part 1 ultrasonic Doppler flowmeters are dealt with from the point of view of instrumentation and theory. This section includes a discussion on possible harmful biological effects, the problem of noise and the functional limitations of the Doppler flowmeter, methods of display and computation and the problems of quantification. In the next sections the uses of transit time instruments to measure organ dimensions and small volume displacements are described, and there follow two sections on the experimental and clinical applications of catheter tip velocity probes and the effects of vascular curvatures and stenoses on the velocity profile. The clinical applications of Doppler instruments in cerebral vascular disease, for coronary artery blood flow measurements, in peripheral arterial disease, in venous disease and for the non-invasive recognition of heart disease are fully discussed.

In contrast to the 389 pages devoted to Doppler ultrasound, flow measurement and experimental applications, the use of pulsed echo for cardiac diagnosis occupies less than 50 pages. Since many would consider this to be the most important and exciting development of ultrasound, the uneven weighting is disappointing to say the least. The section contains only descriptions of two new experimental devices, electro-scan and multi-scan echocardiography, followed by a short section by Edler, the pioneer of cardiac echocardiography, and an even shorter section by Bopp, one of the most active investigators in this field. The final section is a general discussion on the use of Doppler instruments in vascular surgery, on ultrasonic imaging, on venous contamination as a source of error in transcutaneously recorded arterial flow velocities and, strangely, on the determination of myocardial wall thickness by ultrasonic means. These rather disjointed themes have apparently emerged from the final discussion at the end of the symposium.

This book, containing so much which was merely of passing interest at the time when it was discussed, so much which was evolutionary and rapidly changing and so unevenly weighted between flow measurement and ultrasound for cardiac diagnosis, has little to commend it for vascular surgeons or cardiologists wishing to learn more of the techniques, applications and range of cardiovascular ultrasound. It is likely to prove of most value as a momento to those who attended what must have been a stimulating conference on ultrasonic flow measurement. Since the vascular applications of ultrasound are dealt with almost to the exclusion of the cardiac applications and since much of the content concerns theoretical and developmental aspects, the book is likely to find only a limited readership and certainly does not justify its title.

C. OAKLEY

Acupuncture for Physicians

Teruo Matsumoto, Philadelphia. 246×175 mm. Pp. 204+ix, with 148 illustrations. 1974. Springfield, Ill.: Charles C. Thomas. $14.75.

THE object of this short book is to provide sufficiently detailed information for the practising qualified medical practitioner so that he could be in a position to advise his patients on the confused subject of acupuncture, and by his advice perhaps prevent premature and even disappointing results.

The book is divided naturally into three parts by its emphasis on different aspects of acupuncture. The first few chapters deal with the classic acupuncture points, and it is refreshing to see a break from traditional Chinese terminology, in that Professor Matsumoto has produced his own set of anatomically based terms for the median points corresponding to the emerging peripheral nerves. The next few chapters deal with the symptomatic treatment of certain arthritic conditions in an empirical fashion, but with a well-designed protocol. There are no claims made for the reversal of the basic pathology, only symptomatic relief being claimed in the cases described. The third part sets out protocols for biological research work which has to be done in the future to show the efficacy of the procedure in different areas of acupuncture therapy. There is only scant reference to acupuncture anaesthesia, since the author has no practical experience of this subject.

On the positive side of this book, Professor Matsumoto carefully describes experimental conditions and data, even including a detailed description of the apparatus used, so that his work could be repeated or even pre-empted. On the negative side, one is left to wonder if acupuncture really works, and if the objective of the book is to help the doctor advise the confused patient on acupuncture this would be difficult based on reading this book alone. It would be an exceptionally good book on the bookshelf of those interested in experimental acupuncture.

IAN CAPPERAULD

Medical and Surgical Emergencies

Edited John H. Schneewind (deceased), Illinois. Third edition. 175×110 mm. Pp. 434+x. Illustrated. 1973. London: Lloyd-Luke (Medical Books) Ltd. £4·25.

THIS manual was designed originally for use at the University of Illinois hospitals and was initially privately printed. Quite properly, it was considered that it deserved a wider distribution. The third edition has been produced after considerable revision and a change of format for easy readability and quick reference.

The range of emergency situations covered by this manual is far more extensive than its simple title suggests. In addition to the chapters that one would expect in a book bearing this description, there are contributions on, for example, otolaryngologic, ocular and proctologic emergencies. Excellent editing of excellent contributions has produced an informative and well-balanced manual which recognizes all aspects of emergency situations. This is a book designed for both preparation and practice. It should be available in every accident and emergency department and, since it fits very well into the pocket of a white coat, should be a constant part of any casualty officer's equipment. However, its usefulness is not confined to hospital and it is to be recommended to anyone who has to deal with emergency situations occurring in any circumstance. Considering the extent to which this manual is likely to be employed, preliminary reinforcement of the soft covers would be advisable.

D. M. PROCTOR

Flexible Implant Resection Arthroplasty in the Hand and Extremities

Alfred B. Swanson, Michigan. 260×180 mm. Pp. 352+xv, with 552 illustrations. 1973. London: Henry Kimpton. £16·85.

THERE is more to this book than the title would suggest. It is really a treatise on the surgery of rheumatoid arthritis in the arm and hand. It opens with an account of the development of silicones, then leads into a detailed description of the evolution and testing of flexible implants.

Evaluation of results is of vital importance and there is a comprehensive chapter on recording deformity, disability and subsequent improvement after surgery. The large part played by extra-articular deforming forces is stressed and the subsequent need for intensive postoperative splinting emphasized.

The content of the book is rather patchy. There are excellent sections such as evaluation but there are also poor sections. For instance, there is a simple description of the pathology of rheumatoid arthritis, which is surprising in a book concerned with the surgery of the disease. Similarly, the results of finger prostheses are discussed in great detail but those of carpal replacements are rather nebulous.

The book concludes with an extensive bibliography. It is an interesting book reflecting a lifetime's work by Dr Swanson. It should be read by all orthopaedic surgeons and by anyone concerned with the development of implants.

B. A. ROPER

Cryosurgery in Urology: International Symposium in Stuttgart, 1973

Edited H. J. Reuter. 230×155 mm. Pp. 109+ix, with 56 illustrations. 1974. Stuttgart: Georg Thieme Verlag. No price given.

WHEN cryosurgery first attracted the attention of urologists it was for the hope it seemed to hold out of affording a simple and safe means of dealing with urinary obstruction in very old and very unfit men for whom conventional forms of surgery were too dangerous. It was not long before the complications of the treatment were recognized, and to avoid them it became necessary to introduce more and more elaborations on the originally simple theme. The enthusiasts who contributed to this symposium discussed in detail some of these modifications. The bladder may be filled with helium to avoid freezing its wall and the orifices of the ureters; several thermocouples may be introduced per rectum or perineum to monitor the spread of the ice-ball, or the process may be observed through a suprapubic cystoscope. The problem of getting rid of the once-frozen slough may be overcome by performing an endoscopic resection either at the same time as the freezing or a few days later. All of which must make one wonder why endoscopic surgery is not carried out in the first place, and it may be significant that the last section of the symposium is given over to some aspects of transurethral resection which appear to have struck the participants as being new. The outstanding and indeed the most exciting feature of cryosurgery is the hope that it may somehow modify the body's immunological defences against prostatic, and perhaps bladder, cancer. For those who wish to be brought up to date this is a useful and informative symposium which deserves careful study.

JOHN BLANDY

Microbes and Man. A Laboratory Manual for Students in the Health Sciences

Isabel J. Barnes, Sangamon State University, Harry W. Seeley, jun., Cornell University, and Paul J. Van Demark, Cornell University. 275 × 215 mm. Pp. 203 + vi, with 79 illustrations. 1974. Reading: W. H. Freeman & Co. £2·40.

THIS manual is written for students in courses related to nursing and health care.

The authors state that 'a knowledge of basic laboratory techniques of microbiology will serve them well'. In Britain training in laboratory technique is generally considered to be irrelevant except to medical laboratory workers who might find this a useful introductory manual. Nurses armed with culture plates and swabs and guided by a bacteriologist can demonstrate environmental contamination and can test the efficacy of cleaning and sterilization methods; no training in laboratory technique is required. A knowledge of purification methods, identification tests and the use of the microscope will not help them.

This condensed version of a course for professional microbiologists should to be tailored to meet the needs of a different audience. A serious omission is failure to mention any method for testing the efficiency of an autoclave.

E. J. STOKES

Quick Reference to Surgical Emergencies

Edited Gerald W. Shaftan and Bernard Gardner, New York. 235 × 162 mm. Pp. 664 + xvii. Illustrated. 1974. Oxford: Blackwell Scientific Publications. £11·90.

THE editors of this large volume anticipate that it will meet the needs of 'family physicians, emergency physicians, nurses and paramedical staff'. There is a remarkably detailed coverage of every conceivable surgical emergency. Some general chapters, e.g. 'Fluid and Electrolyte Problems', can be read in isolation and provide helpful surveys. Bone and joint injuries are dealt with clearly and each can be referred to quickly. It is less easy to turn up specific abdominal and thoracic emergencies and the diagnosis of these is covered very sparsely. For many conditions, e.g. renal injuries, there are long lists of ancillary investigations, but little indication as to which are the most pertinent and which readily available in the average hospital.

Trainees in surgery or accident work would find it difficult to get balanced views on many of the topics covered, and paramedical staff might only be confused by the elaborate instructions given. However, this is a remarkable 'encyclopaedia' (although the editors deny an intention to produce this!). It is written by acknowledged experts working as a team in one of the busiest hospitals in New York. The book is recommended strongly for the library of the accident and emergency department of all large hospitals but not as a textbook for the surgical trainee. What a pity that in the United States the use of the word 'débridement' is even more confused than with us!

JOHN SHEPHERD

Advances in Cardiovascular Surgery

Edited J. W. Kirklin, Alabama. 234 × 160 mm. Pp. 279 + xiv. Illustrated. 1973. New York: Grune & Stratton. £7·45.

THIS is an excellent and important book which should be on the shelf of every surgeon and physician cardiologist interested in current thought and progress in cardiovascular surgery.

About two-thirds of the book is devoted to congenital heart disease, and this is appropriate as representing the growing edge of advances in the field, with particular emphasis on infant surgery. The remaining sections deal perfectly adequately with valvular heart disease and the important and advancing but less intellectually demanding field of ischaemic heart disease.

As the editor of an outstanding team of contributors, Kirklin's own contributions stand out. Although his somewhat complex classification of congenital heart disease may not be to everyone's taste, it has been widely accepted not only by some of the contributors but by a large number of active surgeons. The section on infant surgery by Kirklin's group is full of important basic principles, but again tends to be too detailed and tabulated and out of character with the rest of the book.

Hard factual data are presented with no woolly statements and, in this respect, it sometimes reads more like a series of scientific publications than a textbook. The reader will, however, appreciate the clear bold sectional subheadings and the good quality of the illustrations, although that on p. 59 appears to be inverted, and on p. 60 the ventricular septal defect is labelled 'D' instead of 'V' which appears in the legend.

In the section on acquired valvular disease an important chapter deals with myocardial protection and function during open heart surgery, and although it does not resolve this current controversy seems to come down on the side of coronary perfusion and the avoidance of prolonged induced ventricular fibrillation.

A great deal of important information is contained in this book and it represents a ready source of current thought and knowledge together with detailed and down-to-earth technical detail. Like many other transatlantic books it is comparatively expensive. However, it would be difficult and laborious to assemble this information from the journals, so that it represents an important volume for all doctors actively engaged in this field.

DONALD ROSS

Handbook of Orthoptic Principles

G. T. Willoughby Cashell and Isobel M. Durran. Third edition. 215 × 135 mm. Pp. 137 + x, with 29 illustrations. 1974. Edinburgh: Churchill Livingstone. £2·25.

The purpose of this book is to provide a handbook on orthoptics for ophthalmologists, an aim which it achieves well besides giving an outline of orthoptics. The book is divided into twelve chapters and gives a useful introduction to the subject of strabismus and anomalies of binocular vision, together with their diagnosis and treatment. Briefly and clearly written, the text contains the basic information essential to the understanding of the subject, but its brevity leaves much detail unmentioned—a feature which makes it inadequate for most orthoptic students but perhaps suitable for young ophthalmic trainees of registrar status desirous of only a superficial insight into the subject. The diagrams are well done but there are not many.

The text has been kept up to date with references to such recent advances as Fresnal prisms and the correction of fixation disparity. In contrast, it is a pity that orbital injuries receive scant mention, and some schools of orthoptics might criticize the treatment advocated for abnormal retinal correspondence.

I. M. DUGUID

Lymphography—Clinical and Experimental

Edited Brendon W. M. Gooneratne, Ceylon. 250 × 190 mm. Pp. 194 + xii. Illustrated. 1974. London: The Butterworth Group. £12·25.

THIS book will be of great value to those studying filariasis and treating patients with Bancroft's filariasis. The chief editor, Dr Gooneratne, reports his lymphographic studies of the genesis of filarial infections in animals. Dr Cahill, Director of the Tropical Disease Center of New York, contributes an authoritative chapter on lymphography in Bancroft's filariasis. It includes a picture of the spectacular labyrinth of vessels seen in the cisternal region of patients with chyluria, from which emanate the incompetent lymphatics leading to the urinary tract and which may be so effectively ligated in the treatment of the disease. Unfortunately, the thoracic ductogram is badly reproduced and reversed left to right. It shows conditions which one now considers abnormal: the dye is still present 24 hours after injection and the duct is dilated and deformed. Such stagnation is undoubtedly a factor in the reflux of chyle.

The remainder of the book deals with techniques, applications, normal radiographic anatomy (which is distinct from classic textbook or cadaver anatomy), secondary and primary lymphoedemas and malignant disease.

Such a short work cannot cover so many large subjects thoroughly, but it remains a stimulating book and, despite imperfections, a source of intellectual pleasure and stimulus.

J. B. KINMONTH

Bronchial Carcinoma

Thomas W. Shields, Chicago, and Roy E. Ritts, Rochester, Minnesota. 225×150 mm. Pp. 181+ix, with 40 illustrations. 1974. Springfield, Ill.: Charles C. Thomas. $12.75.

This book is in the nature of a long essay on bronchial carcinoma. Obviously the authors have much practical experience of the subject but as their work is cast as a review essay it partakes of the disadvantages that this often has. It tends to lack the authority and stimulation that one expects from a personal account, but at the same time it gains from presentation of a critical analysis of the relevant literature, although we note once more the usual habit in an American publication that the review literature is excessively American. The 15 pages of references contain only the equivalent of 2 pages that are not from the United States.

The presentation of the standard accounts of the condition is orthodox and sound. It contains a useful analysis of the indications and limitations of radiotherapy and chemotherapy and of the various attempts at a formal grading of types of bronchial carcinoma and their significance, and for this reason is a useful source of reference. Experience with this disease teaches one that prognosis and curability often depend on some obscure biological factor, and this is opened up by the accounts of immunity and immunotherapy by the second author, Professor Ritts. The introduction of this feature recognizes probably the most important future in the development and the nature of the cure of bronchial carcinoma. One notes certain omissions; thus on p. 115 the 5-year survival rates for pneumonectomy is given from the literature as mostly below 25 per cent with only 2 over 30 per cent, but no mention is made of an article published in 1964 in the English literature of a survival rate of 35 per cent, and the prognosis is not considered beyond 10 years. This is scarcely realistic. The radical types of operation are dismissed casually and with little or no analysis; particularly striking is the virtual dismissal of the great merits of intrapericardial resection.

BROCK

A Manual of Head Injuries in General Surgery

Graham Martin, Wellington, New Zealand. 195×125 mm. Pp. 158. Illustrated. 1974. London: William Heinemann. £2.

This book, according to its preface, is written mainly for 'the general surgeon who has to manage head injuries and the postgraduate student who must sound as though he can'.

The pathology of head trauma, management, the indications for surgical intervention and operative techniques are all presented in a clear concise fashion. It is assumed that the reader will be unlikely to have access to most of the ancillary methods of investigation used in neurosurgical centres and accordingly the use of inspection burr holes is strongly emphasized.

As in all textbooks, not every statement will meet with unqualified acceptance by every knowledgeable reader. The degree to which the administration of steroids influences traumatic brain oedema, for example, and the efficacy of inducing brain expansion by the intraventricular instillation of fluid in the treatment of chronic subdural haematoma are subjects about which unanimity of opinion is lacking in the neurosurgical world. In the present instance such matters, which are not of major importance, are rightly treated in a refreshingly dogmatic manner which in no way detracts from a presentation of head injury management which might well serve as an introduction to the subject for the neurosurgeon in training, while at the same time fulfilling admirably the author's purpose in writing this excellent book.

IAN MCCAUL

Symposium on Reconstructive Hand Surgery. Volume 9

Edited J. William Littler, New York, Lester M. Cramer, Philadelphia, and James W. Smith, New York. 280×220 mm. Pp. 324+x, with 458 illustrations. 1974. London: Henry Kimpton. £20·20.

This is Volume 9 in a series produced by the Educational Foundation of the American Society of Plastic and Reconstructive Surgeons and reports the proceedings of a meeting held in New York, 2–4 November 1972. It includes the deliberations of thirty-five contributors of whom all except three were from the United States. It therefore reflects American thinking and teaching on the subject.

It is a beautifully produced and well-edited book which deals with subjects often omitted or poorly presented in standard textbooks on hand surgery. The volume is divided into nine sections, providing thirty-six short chapters in all (each with a list of references). Each section ends with a report of discussions among those attending (a feature which enlivens the reading matter) which range widely from aetiology and pathogenesis to technical details.

One may question the need for yet another book on hand surgery, but the quality of this volume dissipates any doubts about its academic value. It is difficult to pick out any single chapter for praise when clearly the whole volume has been so carefully edited. Four chapters are devoted to microsurgery, a subject currently in vogue, yet there is a well-illustrated chapter on splints which are still cumbersome and ugly. How long can a tourniquet be left on? Wilgis explains what happens during ischaemia and how to avoid complications.

Indeed, there is something for everyone interested in or actually concerned with surgery of the hand. Despite its excellence the price may preclude many from the purchase, but those who do will have to be prepared to lend their copy and keep a written record of the borrower's name!

JAMES CALNAN

ARMOUR TEMPORARY BIOLOGICAL DRESSING CAN SOLVE THE IMMEDIATE PROBLEM OF TISSUE LOSS COVERAGE AND REPAIR

effective in the treatment of

- partial thickness burns
- debrided full thickness burns
- traumatic skin loss injuries
- soft tissue defects
- decubitus and vascular ulcers

The many advantages of using a biological dressing are

- dramatic reduction of pain
- reduction of fluid and protein loss
- reduction of heat and energy loss
- reduction of infection
- increase in mobility
- protection of exposed tendons, vessels and nerves
- promotion of healing
- psychological improvement of the patient
- improvement of scarring
- In full thickness burns, used as a "test material" to predict the readiness of the granulating bed to accept autograft. This results in a more economical use of autograft material.

Armour porcine skin dressings are presented in sterile lyophilised form, can be conveniently stored without refrigeration and may be reconstituted prior to use in sterile water or balanced electrolyte solution.

Package and size availability is as follows:
Boxes of 5 x 1 sq. ft. roll 3"x 48"
Boxes of 5 x ¼ sq. ft. roll 3"x 12"
Boxes of 10 Patches 2½"x 4"
Boxes of 5 x Wide Strip 8"x 18"
Boxes of 5 x Wide Half Strip 8"x 10"

Full product information on request from
Armour Pharmaceutical Company Limited
Eastbourne Sussex England BN22 9AG

JA6/ABD/5

The single solution

for parenteral nutrition

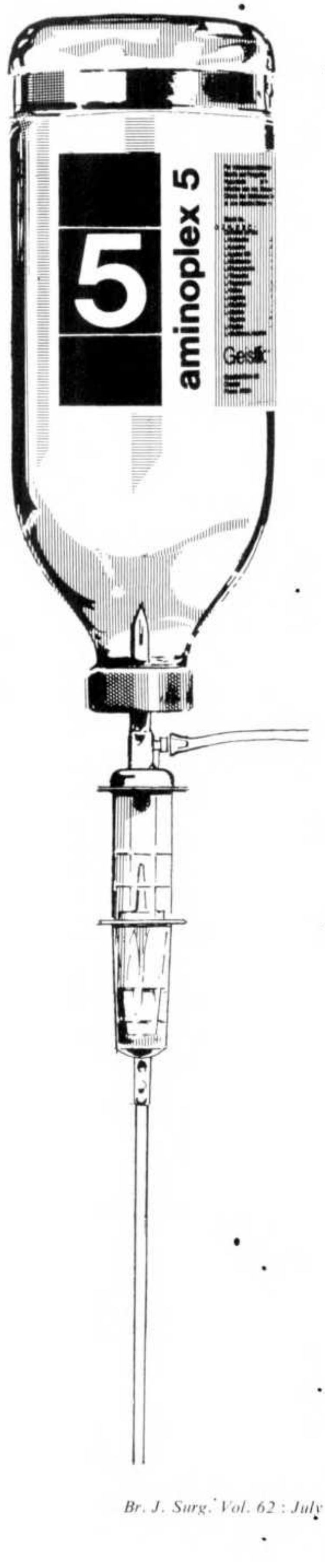
Aminoplex 5

1 litre three times per day provides 15g. of utilisable nitrogen and 3000K calories; the nutrient content being derived from synthetic L-Form amino acids, sorbitol and alcohol.

Geistlich
Chester

In co-operation with Salvia-Werk G.m.b.H., Homburg/Saar, W.Germany.

Medical literature
available from:
Geistlich Sons Ltd.,
Newton Bank,
Long Lane,
Chester CH2 3QZ.
Telephone
Chester 47534-7



Physical Examination of the Surgical Patient:

An Introduction to Clinical Surgery 4/e

By J. Engelbert Dunphy, M.D., Professor of Surgery, University of California School of Medicine, San Francisco, California, and Thomas W. Botsford, M.D., Associate Professor of Surgery, Harvard Medical School.

This fourth edition of **Physical Examination of the Surgical Patient** has undergone extensive revision, and introduces such new emphases as the problem orientated record and pathophysiologic mechanisms of surgical disease. Major changes to this edition appear in the elective examination of the breast, heart, abdomen, and the cancer patient; the emergency examination of the chest, abdomen, and the thermally injured patient. A more clear and concise listing of supplementary readings replaces the old bibliography, and many of the older figures have been replaced with new ones. A second colour plate of epidermal lesions has also been added.

430pp 215 illustrations (2 pages in colour) Cloth binding Price £8.85
Published March 1975

Surgery in the Aged

A title in the series Major Problems in Clinical Surgery

By Lazar J. Greenfield, M.D., Professor of Surgery, The University of Oklahoma Health Sciences Centre College of Medicine, Oklahoma City, Oklahoma.

Approx 250pp Illustrated Cloth binding Approx price £6.65
Publication date September 1975

Atlas of Vaginal Surgery

By Frederick J. Hofmeister, M.D., Associate Clinical Professor, Department of Gynaecology and Obstetrics, Medical College of Winsconsin.

225pp Illustrated Cloth binding Price £8.30 Published January 1975

Surgery of the Trachea

By Hermes C. Grillo, M.D., Massachusetts General Hospital, Boston Massachusetts.

200pp Illustrated Cloth binding Price £7.75 Published January 1974

To obtain your inspection copy, write now to Colin Dann–Publicity Manager, 120 Golden Lane London EC1Y 0TU–Please quote reference WBS 9 with your reply.

W. B. Saunders Company Ltd
12 Dyott Street London WC1A 1DB

SIEMENS

DIATHERMY EQUIPMENT
for modern
ELECTRO-SURGICAL
TECHNIQUES

Available in various designs such as

TROLLEY MOUNTED,
CEILING SUSPENSION
or installation in the
OPERATING THEATRE WALL

Full details available on request

Sierex

SIEREX LIMITED Electro-Medical Department,
Heron House, 109 Wembley Hill Road,
Wembley HA9 8BZ. Telephone 01 903 0418

Branches in Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester, Newcastle and Reading. Agents in Belfast.

The LOR-1A
APPARATUS

CHRONIC TONSILLITIS

successfully treated by ultrasonic therapy

Detailed information available from

V/O MEDEXPORT

31 Kakhovka, Moscow 113461, USSR. Telex 7247
Tel: 121-01-54

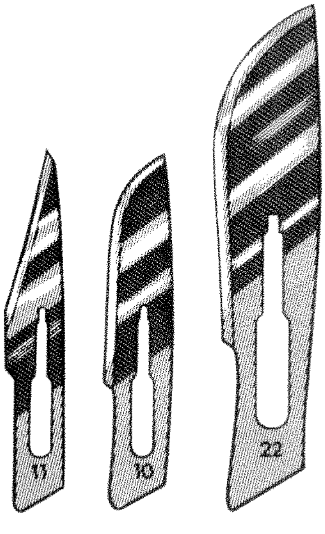
The LOR-1A apparatus produces mechanical vibrations of ultrasonic frequency which have a therapeutic effect on infected tonsils. Clinical tests have shown 75% success in patients treated. Advantages of the LOR-1A are its small dimensions and low weight (less than 5 kg) and its proven safety, reliability and ease of operation. Small ultrasonic generator of low operating voltage permits direct treatment to tonsils.

The operative word is

Swann-Morton

surgical blades

SWANN-MORTON LIMITED. PENN WORKS.
OWLERTON GREEN, SHEFFIELD S6 2BJ. ENGLAND.



GU

NEW

DIATHERMY
FORCEPS,
SCISSORS &
SCALPEL HANDLES
COVERED
WITH
LONG-LIFE..

Insulast

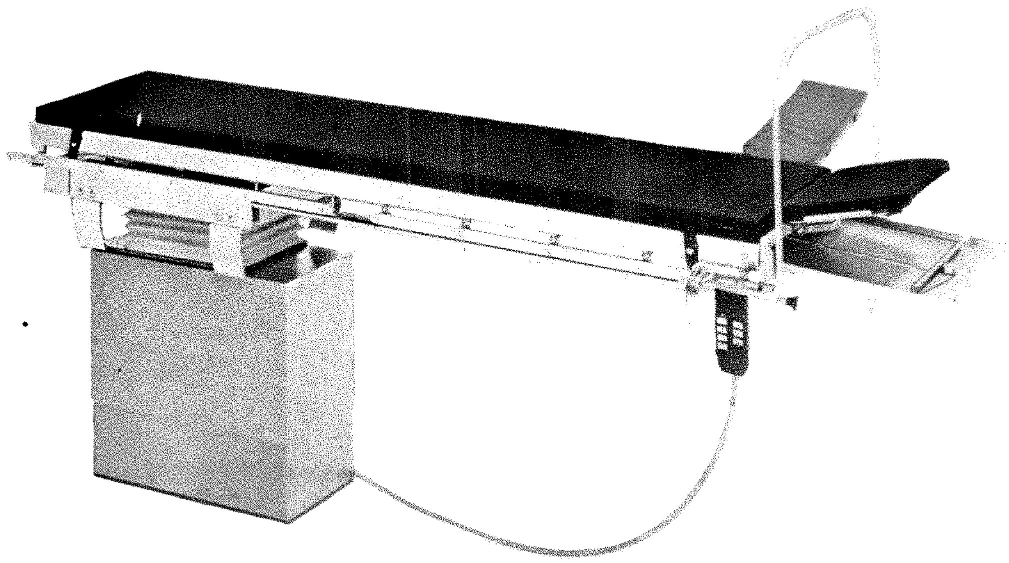
- Developed for autoclaving
- ECONOMICAL · saves on repairs
- SAFER · crack resistant
- THINNER · better grip
- Universal cable fitting

When ordering new diathermy instruments, or requiring old instruments to be re-insulated, always specify 'INSULAST' only obtainable from;

The G.U. Manufacturing Co. Ltd.

28a, Devonshire Street, London, W1N 2AJ
Telephone; 01-935-2835.

Just 4 bolts and a compressed air line



that's all it takes to install the KIFA H3 Table

★ The most advanced operating table system available
★ Reduces patient handling
★ Provides unequalled x-ray facilities ★ Easily cleaned
★ Utterly reliable ★ Quick turn-round of patients
Table tops available for general, urological,
gynaecological, orthopaedic and micro-surgery.
Sierex will be pleased to supply details on request.

Sierex

Sierex Limited
15/18 Clipstone Street, London, W1P 8AE, 01-580 2464
Branches in *Aberdeen, Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester and Reading.*
Agents in *Belfast, Newcastle and Newport.*

CHURCHILL LIVINGSTONE

FUNDAMENTAL TECHNIQUES OF PLASTIC SURGERY—and their surgical applications

IAN A. McGREGOR

1975 Sixth edition 328 pages Illustrated **£6·00**

This book describes the basic plastic surgical techniques, so often passed over by more advanced textbooks, but nonetheless fundamental, with full discussion of the relevance and use of these methods in related specialities. The entire book has been revised, with the chapter on flaps now divided into those with an 'axial pattern' and those with a 'random pattern' according to their vascular characteristics.

TRAUMATIC NERVE LESIONS OF THE UPPER LIMB

Monograph No. 2 of the Groupe d'Etude de la Main

Edited by J. MICHON and ERIK MOBERG

1975 124 pages Illustrated **£8·50**

This is the second of the G.E.M. monographs to appear in English. It deals with one of the most difficult areas in hand surgery, and one in which much international research is taking place. This volume reports the progress of such research and points the way to future developments.

SURGICAL DISORDERS OF THE PERIPHERAL NERVES

SIR HERBERT SEDDON

1975 Second edition 346 pages Illustrated **£12·00**

Although only three years have elapsed since the publication of the first edition, this book has needed revision. Electrodiagnostic investigation has boomed; what are now called entrapment neuropathies have been studied in great detail; the operating microscope has come into regular use; and the scope of autologous nerve grafting—which the author was the first to employ—has been greatly extended.

23 Ravelston Terrace, Edinburgh EH4 3TL

H. K. Lewis & Co. Ltd.

Medical Publishers
and Booksellers

136 GOWER STREET
LONDON, WCIE 6BS

Telephone : 01-387 4282

Just Published . . .
16th Edition of

BAILEY AND LOVE'S
SHORT PRACTICE
OF SURGERY

revised by A. J. HARDING RAINS
and H. DAVID RITCHIE
1308 pp. 1482 Illustrations £10·00 net.

BRITISH JOURNAL OF SURGERY

Binding Cases

Binding cases for Volume 61 may be obtained from the Publishers at £2·00 post free. They are supplied in dark blue cloth with imitation gold lettering on the spine.

If desired, the publishers will undertake the binding at an inclusive charge of £7·50, post free.

JOHN WRIGHT
42–44 TRIANGLE WEST, BRISTOL BS8 1EX

PRE-WAR TOY TRAINS

Wanted for local museum Bing, Hornby and Bassett-Lowke tinplate trains—clockwork, electric or steam, including any accessories however small. Condition is not important as often one piece can be used to restore another. We are aiming to set up as complete a collection of pre-war models as possible, and welcome any relevant items. Reasonable prices paid.

P. B. WHITEHOUSE J.P., Birmingham Railway Museum, 5 Birch Hollow, Edgbaston, Birmingham B15 2QE. *Tel.:* 021 454 7395.

A new concept in surgical lighting
the DAYSTAR
major surgical light

Made in England by

DRAYTON CASTLE
SYBRON CORPORATION

Light Quality The **Daystar** provides cool shadow free colour corrected light giving maximum illumination and minimum heat in the surgical field.

An infinitely variable intensity controller means that you can regulate the level of light to suit your own requirements.

Positioning The **Daystar's** unrivalled ease of mobility puts the light where you want it and keeps it there without drift.

A snap-on autoclavable handle is provided to allow final surgical alignment where necessary.

Supplementary lights
An optional **Orbiter** attachment is available complete with its own intensity controller.

Track lights If you prefer track lighting the **Twinstar** combines **Daystar** quality light with twin track configuration.

Further information
Please complete and return the coupon for further details:

Please provide further details of the Daystar range of surgical lights by: (tick box)

Name__________________ Leaflet ☐
Position__________________ Representative ☐
Address__________________
__________________ Quotation ☐
Tel. No.__________________

Drayton Castle Limited,
Bridge Works, Bentinck Road, West Drayton,
Middlesex. Telephone: West Drayton 43741

staphylocidalpenetrateability!

no other word
is big enough for
fucidin*

'This antibiotic has now established itself as an important antistaphylococcal agent in the treatment of systemic infection. Good absorption and minimal side effects after oral administration combined with an impressive penetration in deep-seated infections gives fucidin an important place in the management of staphylococcal infections.'

* fucidin is a trade mark for sodium fucidate
Further information available on request.
Leo Laboratories Limited,
Hayes Gate House, Hayes, Middx.
L E O

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU

Fight cancer with a will

When testators ask your advice, please remind them of the urgent work of the Imperial Cancer Research Fund. In the Fund's up-to-date laboratories trained minds are using every weapon of modern science to fight all forms of cancer, including leukaemia.

Now one of the world's great research centres, the I.C.R.F. relies entirely on public support. The cancer problem *must* be solved. Please help now.

Patron:
H.M. THE QUEEN
President:
The Honourable Angus Ogilvy

Form of Bequest

I hereby bequeath the sum of....................pounds free of duty to the Imperial Cancer Research Fund, Lincoln's Inn Fields, London, WC2A 3PX for the purpose of scientific research, and I direct that the receipt of the Honorary Treasurer or Secretary shall be a good discharge for such legacy.

Please write for further information to: The Secretary, I.C.R.F. (Dept 164-2),
PO Box 123, Lincoln's Inn Fields, London WC2A 3PX

Lincoln's Inn Fields Laboratories

IMPERIAL CANCER RESEARCH FUND

Vol. 62 : No. 8 : August 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
I. D. A. JOHNSTON Newcastle
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN McADAM Kampala : Uganda
A. C. McEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX

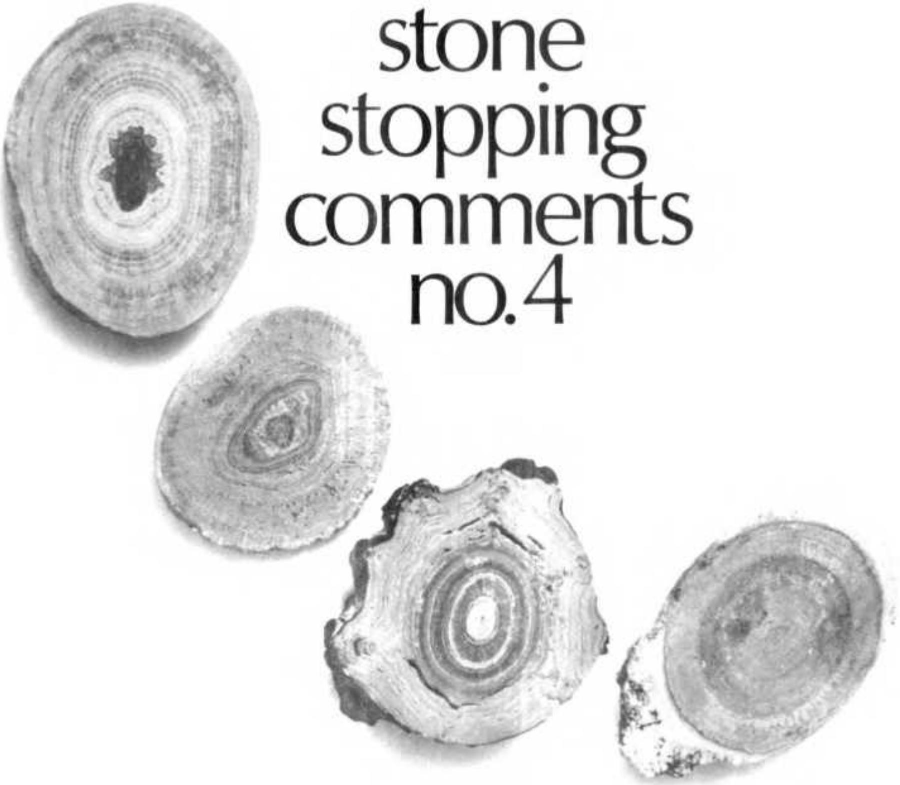
Subscription £15 per annum, post free. Single copies £1·50, post free

---

THE WILLIAMS & WILKINS CO., BALTIMORE

Subscription $36·00 per annum. Single copies $3·00

Second Class Postage paid at Baltimore, and at additional mailing offices.



stone stopping comments no.4

In a recent study[1] measurements of ^{47}calcium and of urinary calcium excretion were made in 125 cases of urolithiasis (78 solitary stone, 47 recurrent).

The authors found that 57 out of 60 patients with hypercalciuria showed raised absorption of ^{47}Ca, whereas 49 out of 106 patients showing similar hyperabsorption of calcium had *normal* calcium excretion. The authors concluded that "... a majority of stone formers, whether they are hypercalciuric or not, absorb calcium excessively from the intestine and this is more prevalent in cases of recurrent urolithiasis."

As a sequel to investigation 1, the same authors[2] studied the effect of Sodium Cellulose Phosphate on intestinal calcium uptake. In comparison to a low calcium, low oxalate diet; "Sodium Cellulose Phosphate can significantly diminish the absorption of calcium from the intestine; there is concomitant diminution of urinary calcium excretion. The plasma levels of the divalent cations do not appear to be influenced by this therapy."

Dosage in this study was varied to evaluate therapeutic effect. "Five grams reduced the intestinal calcium by as much as 85% and even a 1 g dose resulted in a 50% reduction ... Such a dose (5 g), however, is probably essential when it is considered that the substance will ordinarily be dispersed throughout a semi-solid food bolus." Optimum administration time was considered to be 5 g t.i.d. at meal times, or within 1 hour after food.

In terms of side-effects and toxicity, the authors stated "Serum levels of calcium and phosphorus were not altered in any of the patients even when the substance had been taken for a period as long as 7 years in a dose of 5 g 3 times daily." There was no diarrhoea or intestinal disturbance, and patients found SCP reasonably palatable and easy to take.

Presentation

Whitish cream powder packaged in paper aluminium polythene single-dose sachets of 5 g each. Supplied in packs of 100.

References

1 Brit J Urol. (1974) **46**: 377-384.
2 Brit J Urol. (1974) **46**: 385-392.

Whatman
Sodium Cellulose Phosphate

to reduce dietary calcium absorption.

Full prescribing information is available on request.

Whatman®

Whatman Biochemicals Limited,
Springfield Mill, Maidstone, Kent.
Telephone: Maidstone 61688/9 Telex: 96113

The British Journal of Surgery

Vol. 62 : No. 8 : August 1975

Page

Original papers

Observations on peripheral and central temperatures with particular reference to the occurrence of vasoconstriction — Lord Brock, J. M. Skinner and J. T. Manders — 589

Aorto-iliac reconstruction with special reference to the extraperitoneal approach — Raymond Helsby and A. R. Moossa — 596

Oesophagogastrostomy without a drainage procedure in oesophageal carcinoma — I. B. Angorn — 601

Antrectomy with Roux-en-Y anastomosis in the treatment of peptic oesophagitis with stricture — C. M. S. Royston, B. L. Dowling and J. Spencer — 605

Gastric mucosal resection in the treatment of peptic ulcer: a 1–10 year clinical follow-up — R. M. Kirk — 608

Abdominal tuberculosis: demonstration of tubercle bacilli in tissues and experimental production of hyperplastic enteric lesions — Pritam Das and H. S. Shukla — 610

Primary gastric tuberculosis: a case report — R. E. Page, R. E. Williams and E. A. Benson — 618

Congenital hepatic fibrosis: aspects of diagnosis and surgical management — G. S. Sokhi, J. J. Morrice, J. O'D McGee and L. H. Blumgart — 621

Splenic-gonadal fusion — A. K. Pendse, P. N. Mathur, M. M. Sharma and O. P. Gupta — 624

Abdominoscrotal hydrocele — B. R. Parekh, G. Reinboth and O. P. Mishra — 629

Triorchidism with normal spermatogenesis: an unusual cause for failure of vasectomy — M. Hakami and S. H. Mosavy — 633

Immediate operative fitting of upper limb prosthesis at the time of amputation — K. P. Robinson, B. G. Andrews and M. Vitali — 634

The bacteraemia associated with burns surgery — C. H. Beard, C. D. Ribeiro and D. M. Jones — 638

A rabbit model of perforated appendicitis with peritonitis — D. W. King, J. F. Gurry, R. B. Ellis-Pegler and B. N. Brooke — 642

The effect of noxytiolin in experimental peritonitis — D. W. King, J. F. Gurry and B. N. Brooke — 645

Results of modified Robert Jones operation for clawed hallux — E. I. M'Bamali — 647

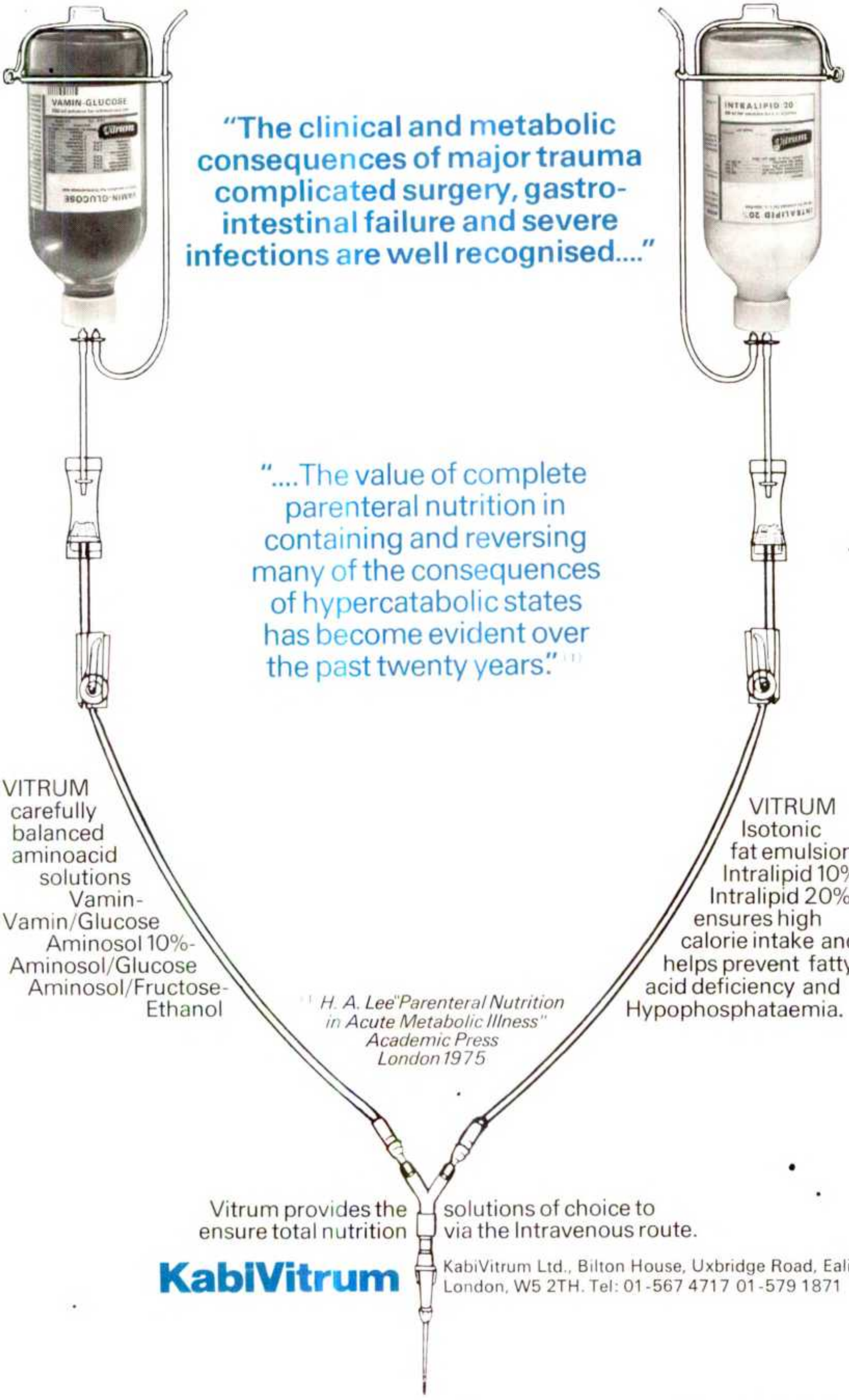
Lymphosarcoma of the breast — Charles F. Ross and Arnold Eley — 651

Surgical Research Society 653

Obituary: Vincent Zachary Cope — 668

Reviews and notices of books 670

© John Wright & Sons Ltd and the respective contributors named above. 1975.
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any other form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.



"The clinical and metabolic consequences of major trauma complicated surgery, gastro-intestinal failure and severe infections are well recognised...."

"....The value of complete parenteral nutrition in containing and reversing many of the consequences of hypercatabolic states has become evident over the past twenty years."(1)

VITRUM
carefully
balanced
aminoacid
solutions
Vamin-
Vamin/Glucose
Aminosol 10%-
Aminosol/Glucose
Aminosol/Fructose-
Ethanol

VITRUM
Isotonic
fat emulsions.
Intralipid 10%
Intralipid 20%
ensures high
calorie intake and
helps prevent fatty
acid deficiency and
Hypophosphataemia.

(1) *H. A. Lee "Parenteral Nutrition in Acute Metabolic Illness" Academic Press London 1975*

Vitrum provides the solutions of choice to ensure total nutrition via the Intravenous route.

KabiVitrum

KabiVitrum Ltd., Bilton House, Uxbridge Road, Ealing,
London, W5 2TH. Tel: 01-567 4717 01-579 1871

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 61. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISEMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

PRESENTATION OF STATISTICS

Authors are reminded that with the frequent use of statistical analysis in biological writing of all kinds it is desirable that:

a. The methods section of a paper should contain a mention of any statistical technique used. If the method is new or unfamiliar either a reference should be given or a description included as a brief appendix.

b. If alternative techniques could have been applied to the data, a short justification of the method is often appropriate.

c. In clinical trials the confidence or tolerance limits of the results should be quoted, particularly when formal statistical significance at the 5 per cent level is only just reached.

d. Abbreviations for statistical terms should follow those used in *Documenta Geigy Scientific Tables*, 7th edition, 1970.

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are two or more authors (apart from the main author), these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated.

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature* (*Lond.*) **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea **4**, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th 3d. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology.* London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BLAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

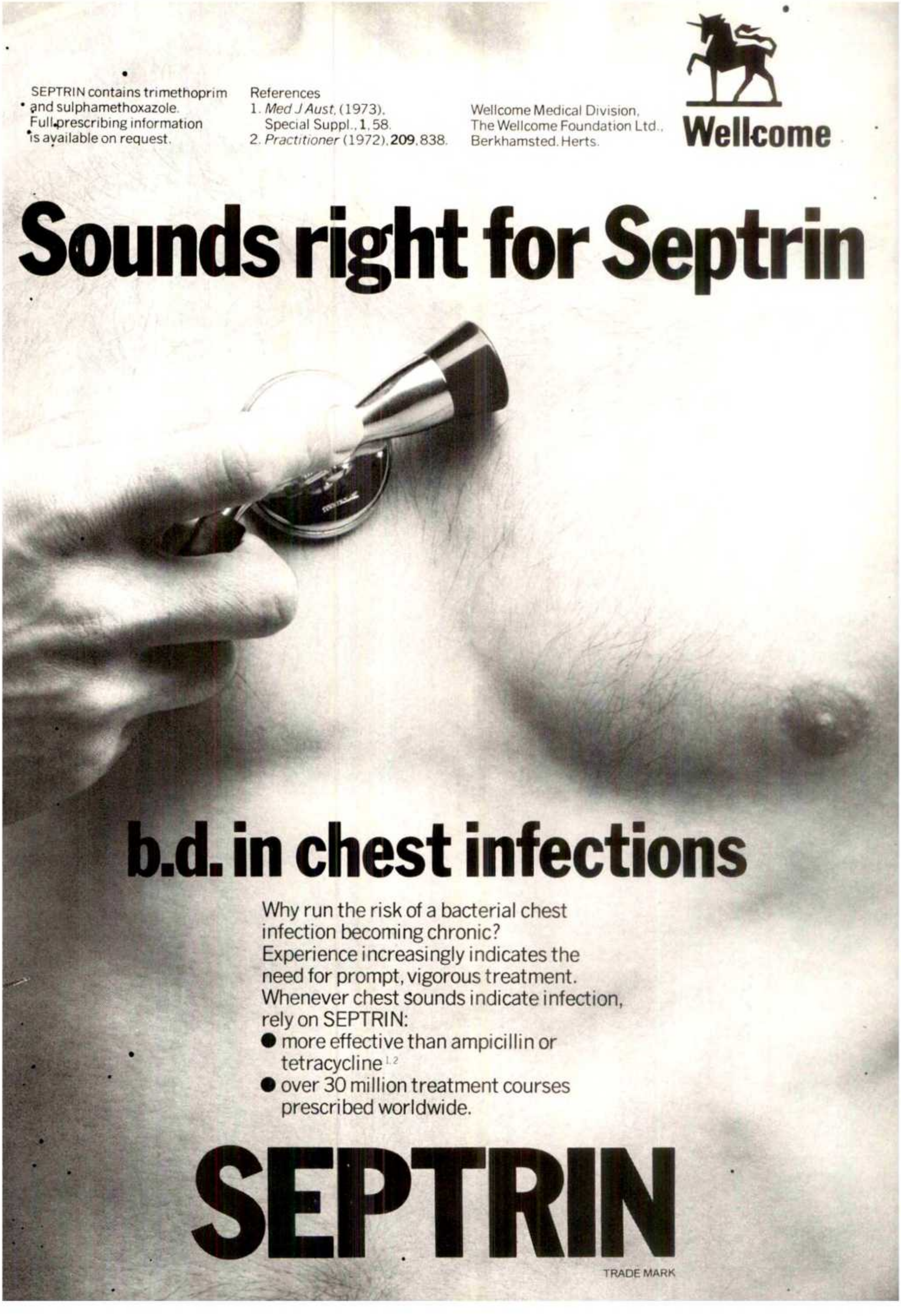
Congress Proceedings

CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding, or that following.

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)



SEPTRIN contains trimethoprim and sulphamethoxazole. Full prescribing information is available on request.

References
1. *Med J Aust*, (1973), Special Suppl., **1**, 58.
2. *Practitioner* (1972), **209**, 838.

Wellcome Medical Division,
The Wellcome Foundation Ltd.,
Berkhamsted, Herts.

Wellcome

Sounds right for Septrin

b.d. in chest infections

Why run the risk of a bacterial chest infection becoming chronic? Experience increasingly indicates the need for prompt, vigorous treatment. Whenever chest sounds indicate infection, rely on SEPTRIN:

- more effective than ampicillin or tetracycline[1,2]
- over 30 million treatment courses prescribed worldwide.

SEPTRIN

TRADE MARK

Forthcoming Titles

AUGUST

Disaster Planning

Proceedings of a Symposium held at the Royal Naval Hospital, Haslar, Gosport, Hants.

Edited by Surgeon Commander J. W. RICHARDSON, OBE, FRCS, RN,
Consultant Surgeon, RN Hospital, Haslar.

These papers, which have been presented by those people recognized as experts in their particular field, discuss many contentious points which underline the need for an agreed policy regarding the management of casualties arising from disaster situations. This book is a 'must' for all those concerned with the formulation of disaster plans: police, fire service, ambulance, doctors (accident surgeons, pathologists), hospital staff, voluntary service, coroners, the media. Those concerned with running nuclear power, industry, the railways, aircraft and ships and the sea.

144 pages   19 illustrations   paper covers   £5·00 net.

SEPTEMBER

Chest Injuries

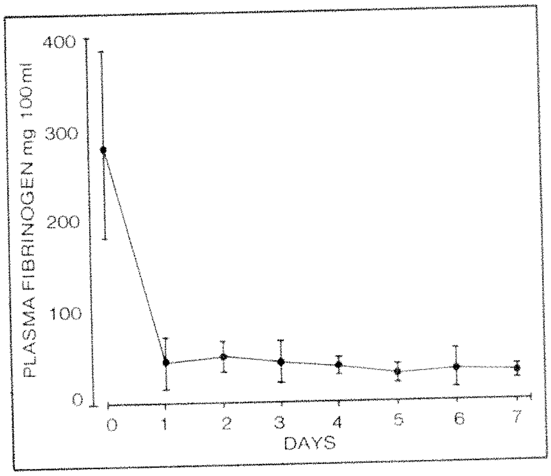
G. KEEN, MS, FRCS, *Thoracic and Cardiac Surgeon, United Bristol Hospitals and Frenchay Group of Hospitals, Clinical Lecturer in Thoracic Surgery, University of Bristol.*

There are many pitfalls of diagnosis and treatment in chest injury that are responsible for avoidable complications and deaths. The book is based on the author's own experience. It will be useful to general surgeons, accident surgeons and anaesthetists and it will also be a practical guide for those who find themselves dealing with a case that is outside their experience.

192 pages   78 illustrations   paper covers   £7·00 net.

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

A new concept in the control of occlusive vascular disease.



Mean plasma fibrinogen level ± SD in 9 patients with venous thromboses. Arvin 2 units/kg body weight intravenously every 12 hours. From Pitney WR. (1971). Thromb Diath Haemorrh, 45, 43.

Its name is Arvin.

This unique drug is now available to specialists, for routine anticoagulant therapy, and to researchers into thromboembolic disorders.

Arvin reduces plasma fibrinogen to a level that maintains marked hypocoagulability without serious spontaneous bleeding complications. This desirable effect is achieved through the specificity of Arvin for fibrinogen—other clotting factors are unaffected.

The consistent does-effect relationship of Arvin allows simple and precise methods of control.

On this basis, we recommend Arvin wherever controlled therapeutic defibrination is desirable.

Full prescribing information, and clinical evidence from studies on the broad range of thromboembolic disorders, are available on request.

Arvin

ancrod

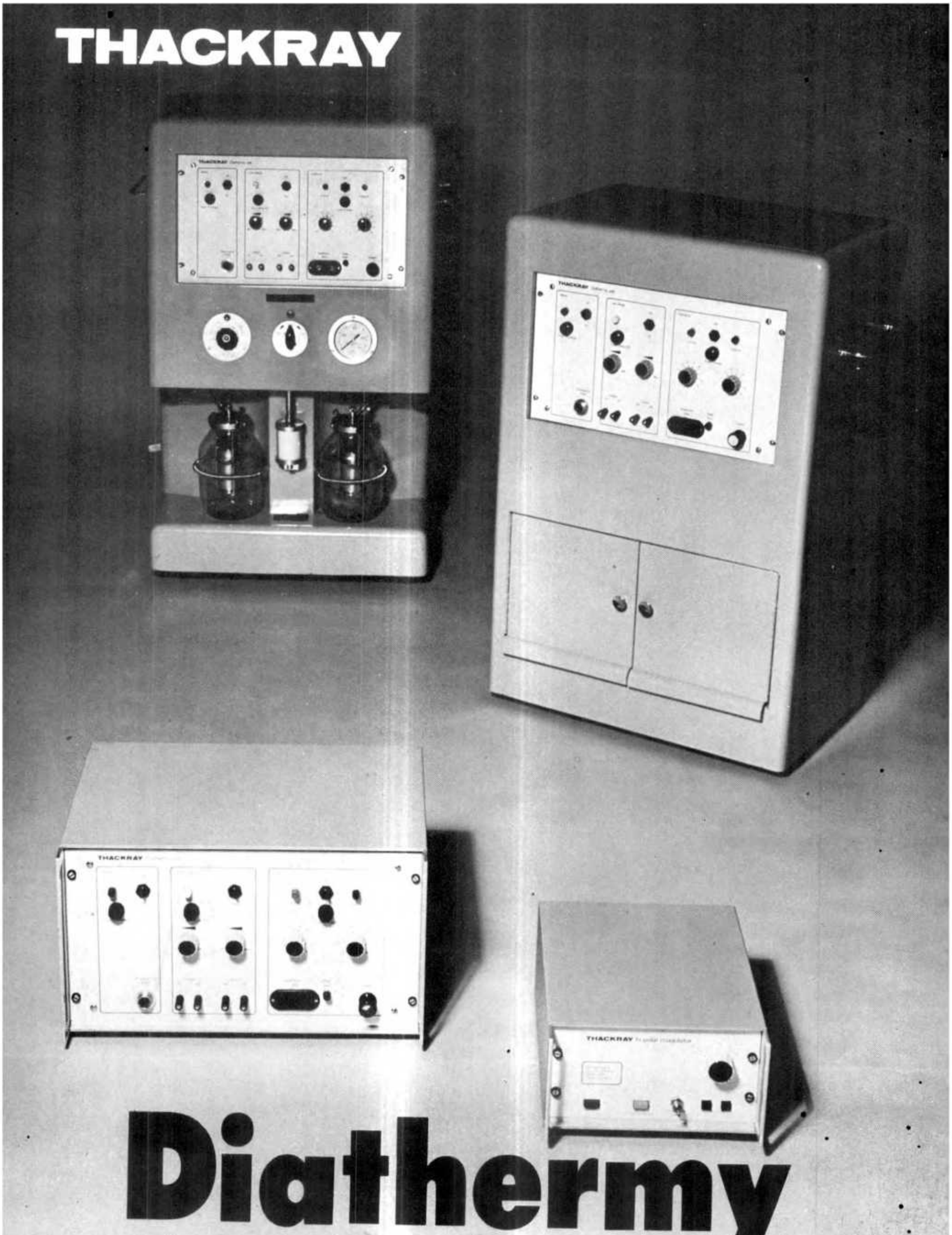
controlled therapeutic defibrination.

Berk Pharmaceuticals BERK Shalford, Surrey.

Arvin is a registered trademark

J4591

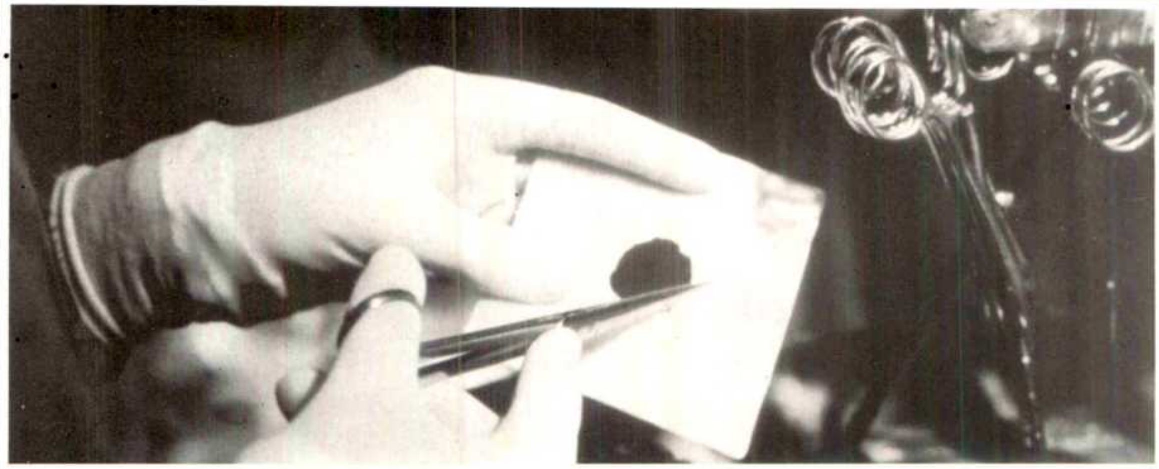
THACKRAY



Diathermy

Thackray Electro-Medical products for the '70's incorporate the latest features in engineering and design, manufactured to a high standard by our technicians, renowned for quality throughout the surgical world. Each of the products illustrated fulfils particular requirements essential to the surgeon. Every item comprises high quality components, being thoroughly and comprehensively tested before leaving our factory.

For further information please contact:



The first word in ostomy management

Skin care after ileostomy, colostomy or ileal conduit starts at the time of surgery itself. Stomahesive protects peristomal skin making the patient comfortable and more confident about his future.

Because Stomahesive contains non-sensitising ingredients, it can be used even on broken, excoriated skin. But why wait for trouble?

Use Stomahesive - right from the start.

Stomahesive, available in boxes of 5 10 cm × 10 cm squares.

Stomahesive is a Squibb registered trademark. Full information available on request to E.R. Squibb and Sons Limited, Regal House, Twickenham TW1 3QT

SQUIBB

The LOR-1A APPARATUS

CHRONIC TONSILLITIS

successfully treated by ultrasonic therapy

The LOR-1A apparatus produces mechanical vibrations of ultrasonic frequency which have a therapeutic effect on infected tonsils. Clinical tests have shown 75% success in patients treated. Advantages of the LOR-1A are its small dimensions and low weight (less than 5 kg) and its proven safety, reliability and ease of operation. Small ultrasonic generator of low operating voltage permits direct treatment to tonsils.

Detailed information available from

V/O MEDEXPORT

31 Kakhovka, Moscow 113461, USSR. Telex 7247
Tel: 121-01-54

THE
2ML AMP
POWER POINT

Genticin Injectable is
supplied as a 2ml ampoule
or vial containing gentamicin
sulphate≡80mg gentamicin
base for adult use and as
a 10mg/ml vial for paediatric use

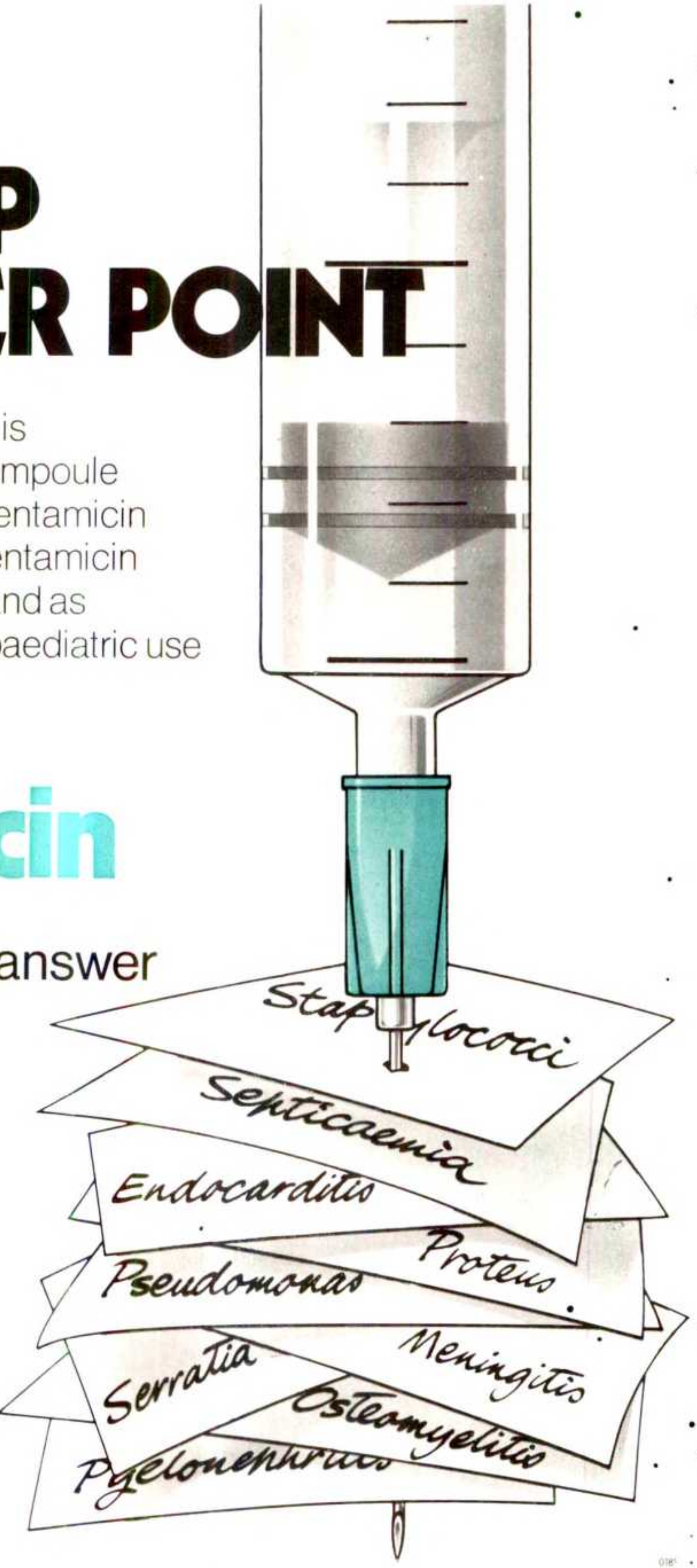
Genticin
injectable
the systemic answer

Full prescribing information is available on request
Nicholas Laboratories Limited
225 Bath Road Slough SL1 4AU
Genticin is a trade mark
PL 0188/5026 Genticin Injectable
PL 0188/5018 Genticin Paediatric
UK Patent No 1021401

Nicholas

Pharmaceuticals, Toiletries
Hospital Supplies

018



The British Journal of Surgery

Vol. 62 : No. 8 : August 1975

Br. J. Surg. Vol. 62 (1975) 589–595

Observations on peripheral and central temperatures with particular reference to the occurrence of vasoconstriction

LORD BROCK, J. M. SKINNER AND J. T. MANDERS*

SUMMARY

The importance is emphasized of the inadequacy of the term 'body temperature', but that both core temperature and the peripheral temperature must be considered. The assessment of vasoconstriction is informative, and advantage should be taken of the exact information that can be provided by an electro-thermometer as opposed, for example, to a touch of the hand. The core temperature is taken from the rectum, the nasopharynx or tympanic membrane, and the peripheral temperature from the great toe.

If the peripheral temperature falls the loss of body heat is prevented and the core temperature rises. If this is not understood or not recognized misguided attempts may be made to try to reduce the raised central temperature by cooling the skin. This can result in a further rise of central temperature. The recognition of peripheral vasoconstriction enables a proper assessment to be made of its basic cause and of the necessary treatment.

The most important cause is hypovolaemia from blood loss and a detailed account is given of how this should be recognized, especially by a study of the gradient between central and peripheral temperatures. Such studies should be a routine in any severe illness, whether medical or surgical, in which circulatory deterioration is likely, especially after major operations or injuries.

Study of the temperature of the heel (hindfoot) as well as of the toe (forefoot) can indicate a selective 'shutdown' of peripheral circulation that reveals an especially critical circulatory state.

THE results are presented of studies on the effects on body temperature of environmental and of internal factors, especially in relation to differences between the peripheral and the central or core temperature. The subject is large and complex and turns chiefly on the development, causation and significance of peripheral vasoconstriction. Much can be learned from a study of vasoconstriction, and the peripheral temperature has been used as a means of measuring this important mechanism. It should no longer be thought sufficient to judge what is happening to the skin temperature by a simple touch of the hand. Sensitive electro-thermometers enable the measurement, with considerable accuracy, speed and advantage, of fluctuations in this valuable and important parameter. Such methods have hitherto been largely neglected. The temperature of the skin is essentially an indication of the resultant between the degree of patency (constriction versus vasodilatation) of its vessels and of the flow and pressure of the circulation to it. Vasoconstriction of skin vessels can be via an axon reflex or as part of general sympathetic activity.

It is necessary to emphasize that it is not enough to speak of 'body temperature', but that both the core temperature and the peripheral temperature must be considered. The core temperature can be measured from the rectum, from the nasopharynx, from the lower one-third of the oesophagus or from the tympanic membrane, although each site may have disadvantages or slight differences. The peripheral temperature is measured from the ball or the side of the big toe but valuable information can also be obtained by measuring the temperature of the hindfoot (heel). If there is general body cooling the temperature at each of these sites, central and peripheral, will fall together (*Fig.* 1). Under anaesthesia the thermoregulatory mechanism becomes paralysed and the subject behaves poikilothermically. In the intact homeotherm when the core temperature falls beyond the tolerance of the 'thermostat', peripheral vasoconstriction occurs to limit heat loss from the body and this persists until the core temperature is restored. As the peripheral temperature falls the central temperature may rise (*Figs.* 2, 3). This is due to peripheral vasoconstriction limiting the loss of body heat and thus the core temperature rises as a result of the continuance of body metabolism. The rise may be

---

* Department of Surgical Sciences, Royal College of Surgeons, London.

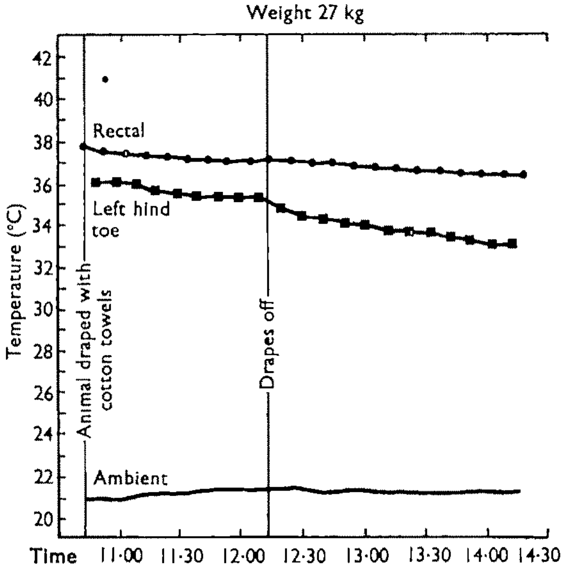


Fig. 1. With general body cooling the central and peripheral temperatures fall together.

even greater if shivering occurs and may reach an important degree of hyperpyrexia (e.g. 40 °C or even higher).

If the rise in body temperature is general (as in a febrile illness) and is accompanied by the hot, flushed skin of vasodilatation, then the practice of trying to reduce the high temperature by some form of surface cooling, such as tepid sponging, is acceptable. However, if the presence and the significance of a cool or cold skin due to vasoconstriction is not appreciated and that the rise in central temperature is due to it, the high central temperature may be allowed to dominate the clinical picture and misguided attempts may be made to try to reduce it. These attempts will consist essentially of applying cold in some form to the skin, such as tepid or cold sponging or by directing a stream of cold air over the body from a fan or simply by exposure to a draught such as from an open window, or the thermostat of an air-conditioned room may be turned down several degrees. Applying cold to the skin fails to extract heat and indeed increases the constriction of the skin vessels. *Fig.* 3 shows how the attempt to reduce 'body temperature' in this way not only fails but results in it rising even higher. This is,

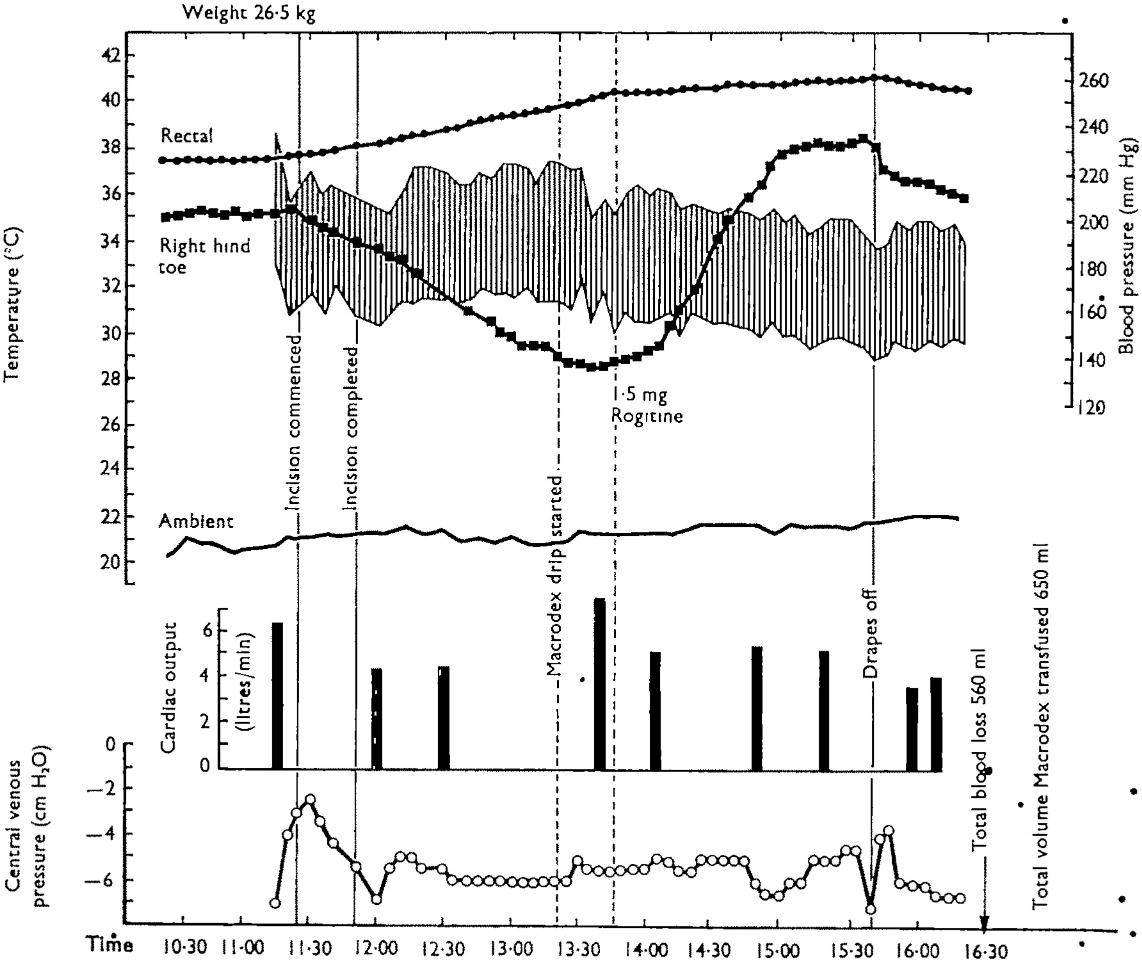


Fig. 2. With a fall in surface temperature from peripheral vasoconstriction due to blood loss the central temperature rises, in this case to over 40 °C. Correction is seen to occur when blood loss is replaced and vasodilatation is encouraged (by Rogitine).

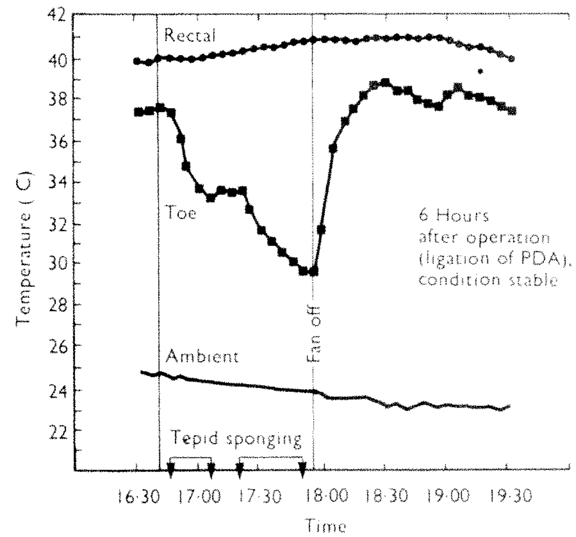


Fig. 3. The misuse of tepid sponging and a fan in an empirical attempt to reduce a raised central temperature of 40 °C. The skin temperature fell to below 30 °C. The skin temperature rose and the central temperature fell when the tepid sponging and the fan were stopped. PDA, Persistent ductus arteriosus.

in fact, a demonstration that tepid sponging and similar methods not only fail when the true situation is not recognized but actually aggravate the condition. The only logical measure is to produce peripheral vasodilatation which will permit increase of heat loss from the skin and hence lowering of the core temperature (*Fig.* 4). In other words, both doctors and nurses should be taught that in the absence of a warm flushed skin it is wrong to try to reduce temperature by some empirical method. Not only is it wrong treatment but the clinician reveals that he has failed to grasp the significance of the cold skin that should point the way to some cause other than 'fever' for the raised central temperature. He has missed the chance of elucidating what is really wrong with the patient.

There are a number of causes for peripheral vasoconstriction and the cold skin that results. When in an equable environment peripheral vasoconstriction is exhibited by a low peripheral temperature and the 'core' temperature is raised above normal, then it is likely that the peripheral vasoconstriction is due to a non-thermoregulatory cause. The very important one to consider is hypovolaemia from any cause, but especially from blood loss. This provides the primary cause for a vasoconstriction which is due to a fall in cardiac output as a result of diminished venous return and hence stimulation of the aortic mechanoreceptors that initiate peripheral vasoconstriction. It is necessary to sound a note of warning, for if this vasoconstriction is treated solely by the exhibition of vasodilators the result can be disastrous and even fatal because a sharp fall in systemic blood pressure results from an increase in the arteriolar and capillary bed (*Fig.* 5). The hypovolaemia must first be corrected by transfusion and only then is it safe to establish vasodilatation. Examples of this have been given in earlier articles (Spitzer and Brock, 1968; Ross et al., 1969, *Fig.* 6) and an example is given in *Fig.* 7. If the cause of an important gradient between the central and peripheral temperatures is hypovolaemia, additional information will be provided by measurement of the central venous pressure (which will be low), a low urinary output and perhaps a low arterial pressure and raised pulse rate (*Figs.* 5, 6). However, it should be noted that peripheral vasoconstriction assessed by temperature records is a more sensitive indicator of hypovolaemia and can provide evidence

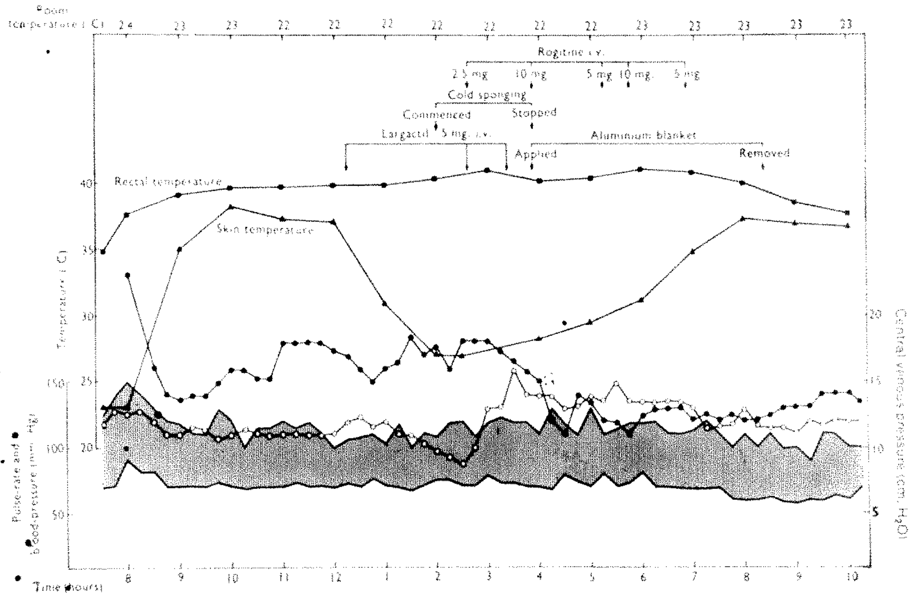


Fig. 4. Central heat retention. Treated empirically by cold sponging which aggravated the peripheral vasoconstriction and the rise in rectal temperature. The response to administration of an α-adrenergic blocker (Rogitine) is well shown and was fully satisfactory.

of this even when blood pressure and central venous pressure remain within normal limits. If the cause of the hypovolaemia is blood loss this can also be reflected in the haematocrit and the haemoglobin levels. It is lamentable, even pathetic, that in spite of such rich clinical changes which should tell their tale, misguided attempts should be embarked upon to reduce a raised central temperature by empirical methods that ignore a scientific assessment of the true situation. In such a case the information given by a study of the gradient between the central and the peripheral temperatures is informative, is more sensitive and should always be used.

There are other causes of hypovolaemia than haemorrhage, as for instance in various dehydrating conditions. Temperature studies can be of great value in any severe illness, medical or surgical, in which circulatory deterioration is likely to occur, or is actually occurring. An example of this is phaeochromocytoma (Brock, 1975) in which severe hypovolaemia may be present, is made worse when operation is done and may be wrongly treated by the use of vasoconstrictors (such as noradrenaline) in a misguided attempt to support the failing circulation when what is needed is transfusion to correct the hypovolaemia.

Hypovolaemia may be aggravated by the pooling of blood within vessels apart from actual haemorrhage. This is why important hypovolaemia is an accompaniment of certain major operations and a plea is

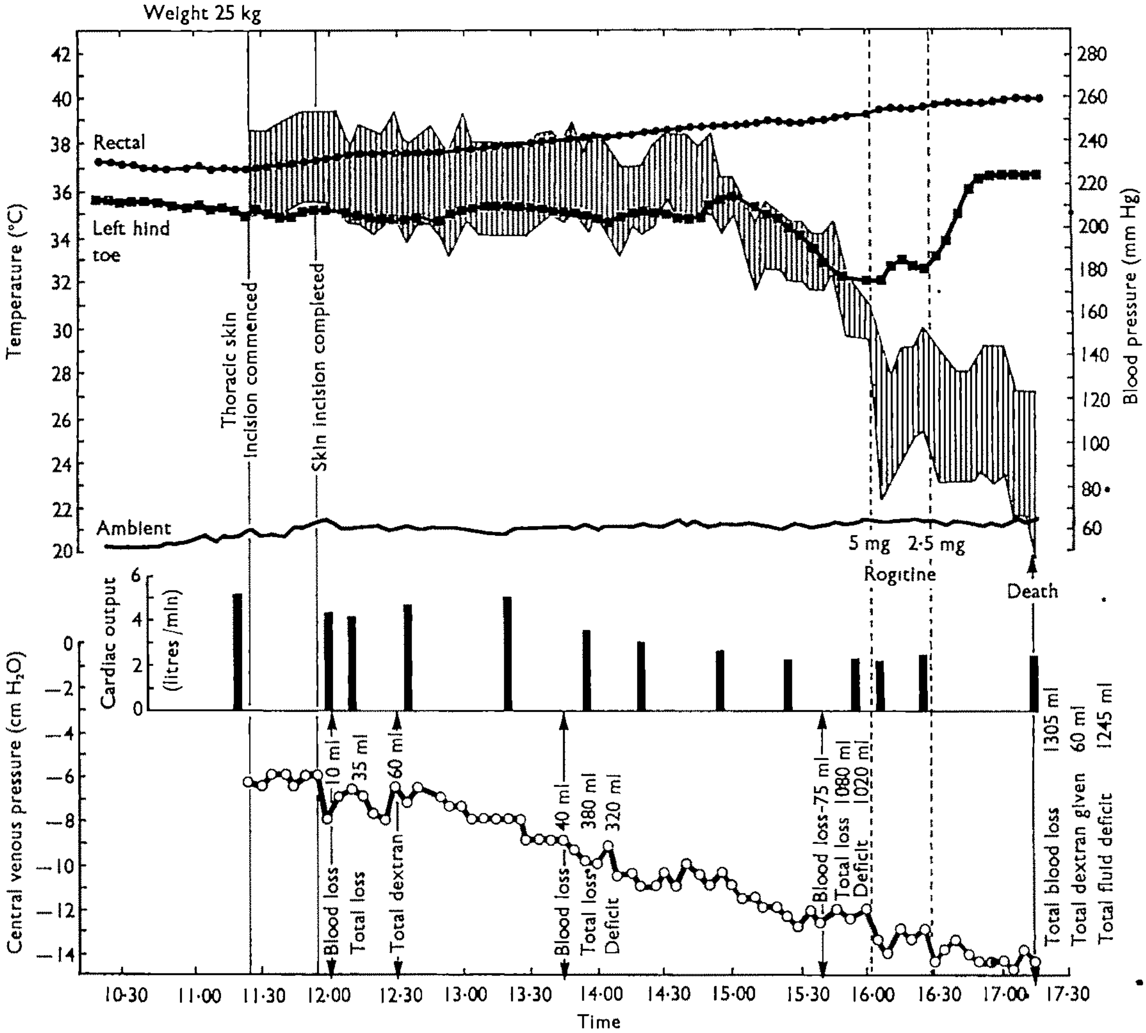


Fig. 5. The effect of blood loss (1080 ml) and inadequate replacement by only 60 ml. Estimated blood volume = 2350 ml. By 16.00 hours the toe temperature had fallen to 33 °C and the rectal temperature rose to 39·5 °C. The blood pressure had fallen from 240/200 to 160/140 mm Hg and the central venous pressure had fallen from −6 to −12 cm H_2O. At 16.00 and 16.30 hours two doses of Rogitine, 5 and 2·5 mg, were given, resulting in a rise in the toe temperature to 37 °C and a levelling off of the rectal temperature. This was accompanied by a sharp fall in blood pressure to 130/70 mm Hg and a fall in central venous pressure to −14 cm H_2O. The total blood loss by 17.30 hours had reached 1305 ml, a deficiency of 1245 ml (nearly 50 per cent of blood volume). At this time the blood pressure fell right away and death occurred suddenly. This demonstrates well the lethal effect of causing peripheral vasodilatation in the absence of replacement of blood loss.

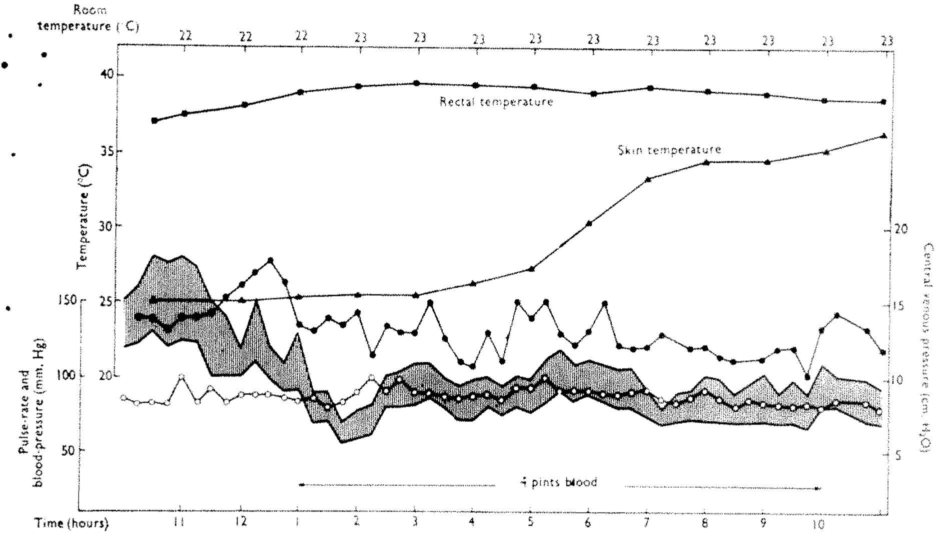


Fig. 6. Severe hypovolaemia and prolonged vasoconstriction following aortic valve excision and replacement. Note the concomitant fall in blood pressure and the low venous pressure. It was necessary to give 2·4 litres of blood before a stable thermal state was achieved. Blood replacement should have been begun earlier and more massively and should have been accompanied by a vasodilator drug (chlorpromazine). (Ross et al., 1969.)

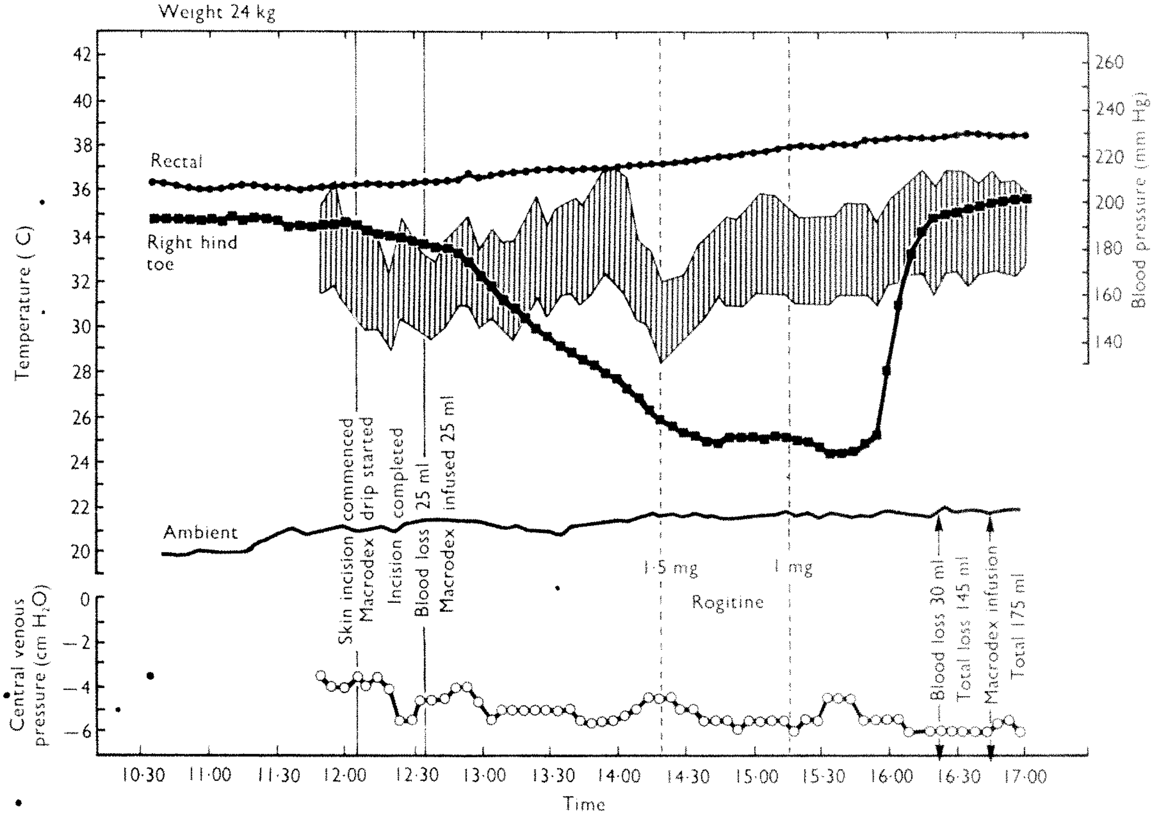


Fig. 7. The effect of an incision and blood loss in causing severe peripheral vasoconstriction (toe temperature 25 °C) and a rise in central temperature to 38 °C (gradient 13 °C), uncorrected by replacing the measured blood loss but completely corrected by Rogitine. The toe temperature rose to 35·5 °C and the central temperature flattened out at 38·5 °C (gradient reduced to 3 °C). This was supported by Macrodex infusion of 175 ml to correct the total blood loss of 145 ml. Contrast with *Fig.* 5 in which no infusion was given to support the vasodilatation caused by Rogitine.

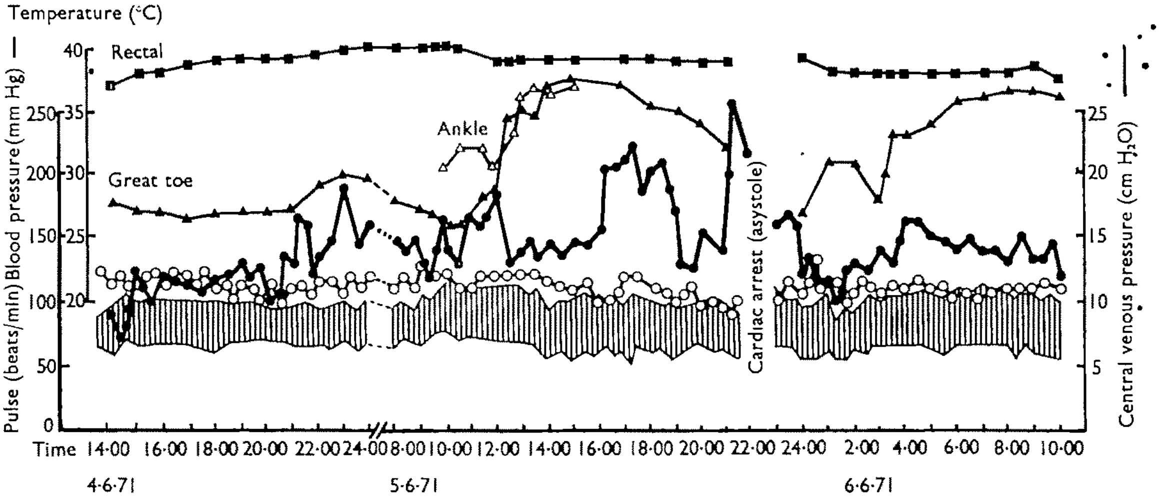


Fig. 8. The postoperative course following mitral valve excision and replacement. Initially there was a substantial gradient of 13 °C between the rectal temperature (40 °C) and the toe temperature (27 °C). The patient was not hypovolaemic as careful blood loss and replacement had been observed. On the morning after operation it was noticed that although the toes and forefoot were cold the heel and calf were warm. The heel or ankle temperature was then recorded and found to be 32 °C. As soon as the patient was extubated the toes became warm, the toe and heel temperatures both rose to 36 °C and the rectal temperature fell to 39 °C. This illustrates that selective peripheral vasoconstriction can occur and indicates an inadequate circulation. Subsequently, ventricular fibrillation occurred but responded to treatment. *See* text for further details.

made for the detection of this by using temperature studies. It is especially liable to occur after open heart operations, when in addition to frank blood loss there may be gross mal-distribution of fluid within the various body compartments. The success or failure of such critical operations may depend greatly on awareness of and detection of signs of significant hypovolaemia. Matthews et al. (1974a, b) have written of this and Matthews has also coined the phrase 'cold feet in cardiac surgery' that is based on the vasoconstriction that results and study of which can be such a valuable indication of what is happening in the critical state present. Matthews et al. proposed a simple nomogram based on the 'warm-up' time in 81 'normals' showing a consistent warm-up pattern which is independent of potential variables and that can be used in postoperative treatment. They claimed that this has become an indispensable part of routine postoperative care in their unit and they regarded it as the simplest and most effective available method of monitoring the circulation. From our own observations and experience over many years we agree with these conclusions.

It is also possible to show that there can be a selective control of peripheral temperatures if, in addition to the temperature of the forefoot as shown by the big toe, the temperature of the hindfoot is observed from the inner side of the heel or ankle. The potential significance of this is best illustrated by observations on a specific case.

Case report

Mrs R. A., aged 36 years, had an excision and replacement of the mitral valve because of severe regurgitation. As can be seen from *Fig.* 8, there was a substantial gradient between her central temperature (40 °C) and her toe temperature (27 °C). She was not hypovolaemic, careful fluid and blood replacement having been observed. On the morning after operation it was noticed that although the toes and forefoot were cold the heel and calf were warm. At 10 a.m., therefore, the heel or ankle temperature was recorded as well as that of the toe or forefoot and was found to be 32 °C. There was no anatomical cause for the cool forefoot and its poorer circulation, although the pedal pulses were small. As soon as the patient was extubated both the toe and heel temperatures rose sharply to 36 °C and the rectal temperature fell to 39 °C, as can be seen from the chart at noon (*Fig.* 8). The change in the forefoot and toes was striking; they were now warm and flushed and the pedal pulses were full and bounding. This change confirmed that the earlier discrepancy in the peripheral circulation was due to more severe distal vasoconstriction, a selectivity resulting from a deficient cardiac output that made it necessary for the body to shut down some of the peripheral circulation. In other words, a study of the toe, heel and rectal temperatures pointed to the precarious state of the circulation. Throughout the afternoon the improved peripheral circulation was reflected in the temperatures that continued at 37 and 35 °C, a normal gradient. During the early evening, as *Fig.* 8 shows, the toe temperature began to fall, the central venous pressure rose to 35 cm and the urinary output fell. Tamponade was suspected but there was a good response to Lasix and the central venous pressure fell to 21 cm. The toe temperature, however, fell to 32 °C and there was clear evidence of cardiac distress. This was confirmed when at 10 p.m. ventricular fibrillation and cardiac arrest occurred. Fortunately this responded to resuscitation. The gradient between the central and peripheral temperatures was still present but it lessened as her general condition improved and by early morning it had disappeared. Her circulatory state appeared stable, the toes were hot and the pedal pulses bounding and she made a good recovery.

This event led to us making a routine assessment of the heel as well as of the toe temperature because we felt that this enabled a more delicate assessment to be made of degrees of deficiency of the peripheral circulation. In fact, it could demonstrate a peripheral shutdown that indicated the inability of the body to maintain a full circulation. Soon after this another similar case presented, that of a young woman aged

24, also with severe and long-standing mitral regurgitation for which valve excision and replacement were necessary. In this case, however, the deficient toe and forefoot circulation, as demonstrated by the lower temperature in contrast to the ankle and calf temperatures which were warm and satisfactory, did not improve, indicating that the circulation was not capable of improvement, and death followed. Other similar instances have been observed and it has become clear that richer and more significant information about the circulatory state can be obtained from study of selective regions of the peripheral circulation. It can, of course, be tedious to take the temperature at many sites and little extra information may be obtained. Some people have in fact advocated study of the great toe temperature alone as a measure of a shock-like state (Matthews et al., 1974a, b). We feel that this can be incomplete, and in any event in managing a severely ill patient, especially after cardiac surgery, the extra information to be obtained for instance from the heel is invaluable. It has been stated that the temperature of the medial aspect of the thigh gives the average skin temperature (Teichner, 1958), and that this measurement on its own is sufficient. We cannot agree with this because it does *not* estimate peripheral vasoconstriction. This cannot be assessed by an average reading from a more central site.

Although great care may have been taken to measure and to replace blood loss, it is often found after a severe operation that the circulatory state does not improve until an additional 1, 1½ or even 2 litres of blood have been given as well as the measured blood loss (*Fig.* 6). Presumably this is because of pooling of blood in certain areas that causes a loss of effective circulating blood volume. It is in such cases that study of central and peripheral temperatures is particularly valuable and informative.

At the same time we must realize that although 'blood loss' in the widest sense may be the chief cause of a circulatory deficiency and of peripheral vasoconstriction, it is clearly important to study and to comprehend other causes of peripheral vasoconstriction if reliance is to be placed upon the temperature findings which they determine. In other words, what factors may be responsible for peripheral vasoconstriction and thus for a fall in toe temperature? This will be the subject of further communication.

Acknowledgements

This work was carried out with the help of a grant from the Department of Health and Social Security to which acknowledgement is due. We wish also to thank Mrs Christine Mills and Miss Catherine Richardson for valuable technical assistance.

References

BROCK, LORD (1975) Hypovolaemia and phaeochromocytoma. *Ann. R. Coll. Surg. Engl.* **55**, 218–221.

MATTHEWS H. R., MEADE J. B. and EVANS C. C. (1974a) Peripheral vasoconstriction after open heart surgery. *Thorax* **29**, 338–342.

MATTHEWS H. R., MEADE J. B. and EVANS C. C. (1974b) Significance of prolonged peripheral vasoconstriction after open heart surgery. *Thorax* **29**, 343–348.

ROSS B. A., BROCK, LORD and AYNESLY-GREEN A. (1969) Observations on central and peripheral temperatures in the understanding and management of shock. *Br. J. Surg.* **56**, 877–882.

SPITZER A. G. and BROCK, LORD (1968) The recognition of hypovolaemia after open heart surgery. *Guy's Hosp. Rep.* **117**, 1431–138.

TEICHNER W. H. (1958) Assessment of mean body surface temperature. *J. Appl. Physiol.* **12**, 169–176.

Br. J. Surg. Vol. 62 (1975) 596–600

Aorto-iliac reconstruction with special reference to the extraperitoneal approach

RAYMOND HELSBY AND A. R. MOOSSA*

SUMMARY

We have used the extraperitoneal approach for aorto-iliac reconstruction for lower limb ischaemia in over 130 patients. The operative exposure is excellent. Operating time is shortened and the upset to the patient much less than in the transperitoneal approach. We now believe that the method is suitable for use in the majority of aorto-iliac reconstructions. Patency rate 4 years after surgery for claudication is 89 per cent.

THE satisfactory results of aorto-iliac reconstruction are well documented in communications from many centres in different countries and stem from the pioneer work of Dos Santos, Rob and Eastcott, de Bakey, Cannon and Linton, to name but a few. Taylor (1973) has provided a valuable and realistic review of the scope and limitations of reconstructive arterial surgery and his comments and observations accord with our own experience. It is well recognized that in patients with a combination of femoropopliteal and aorto-iliac occlusive disease an aorto-iliac reconstruction will frequently increase the flow to and through the profunda femoris artery sufficiently to improve claudication or to save the limb from major amputation. When the disease is mainly confined to the aorto-iliac region, one can offer the patient a very high prospect of complete and lasting relief.

It would seem to the authors that no useful purpose can be served in reporting the detailed follow-up of further patients who have undergone aortic reconstructive operations unless the results are significantly better (or worse) than those in other series. This communication adds little to the existing store of information on postoperative results but seeks to influence surgeons to modify their technique.

As the proportion of our population over the age of 65 increases and since atherosclerosis is such a common disease, it is likely that the number of patients presenting for reconstructive surgery will continue to increase. The size of the load must inevitably mean that, as with urology, much of the work will need to be done by the general surgeon. Inevitably, the number of successful reconstructive operations will be approximately balanced by the need for major amputation in other patients, and it is the authors' belief that the same surgeon should accept equal responsibility for both groups. The purpose of this report is to emphasize that aorto-iliac reconstructions can be adequately performed by general surgeons trained in vascular surgery, and to underline the advantages and the ease of the extraperitoneal approach. This approach is by no means new. Rob wrote of it in 1963 and recalled that Astley Cooper had described it in *Guy's Hospital Reports* in 1836. It was recommended by Stipa and Shaw (1968), Douglas (1973) and Martin and Marston (1973); nevertheless we believe that it is still not widely used by surgeons doing vascular work. We have found the exposure quick and convenient, the general upset to the patient far less marked than in the transperitoneal approach and the incidence of postoperative distension, wound dehiscence, incisional hernia and chest complications negligible. Obesity is not a contraindication but rather an indication for the use of this approach. For these reasons the extraperitoneal exposure has become our method of choice and is now used in the majority of aorto-iliac reconstructions. Preoperative assessment does not differ from that used elsewhere, except perhaps that preoperative arteriography has not always been done. In particular, if a patient presents with severe rest pain or gangrene and has an absent femoral pulse on the affected side, when the contralateral femoral pulse is present, operation might well be undertaken without a preoperative angiogram.

In the years 1961–74, 330 aorto-iliac reconstructions were performed for lower limb ischaemia. During the same period 250 femoropopliteal reconstructions, over 500 lumbar sympathectomies and 375 leg amputations were done. In addition, about 800 nonvascular operations including routine urological and gastro-enterological procedures were performed each year on an undergraduate teaching unit consisting of 2 consultants, 1 senior registrar, 1 junior trainee registrar and 1 house surgeon at the Liverpool Royal Infirmary. About 90 per cent of the arterial operations were done by one surgeon.

Three basic operations—aorto-iliac disobliteration, aortofemoral bypass and, less frequently, iliofemoral bypass—were used. If the external iliac arteries were grossly diseased the problem was usually managed by an aortofemoral bypass graft rather than by disobliteration. The graft material used has been in nearly every case woven Dacron. Knitted velour Dacron has been used for iliofemoral grafts, but it is not yet available as a bifurcation. The anastomosis of graft to aorta has been either end to end or end to side—approximately an equal number of each. Prophylactic broad spectrum antibiotics (usually ampicillin) have been used routinely, being started a

---

* The Royal Infirmary, Liverpool.
Present address of A. R. Moossa: Department of Surgery, University of Chicago.

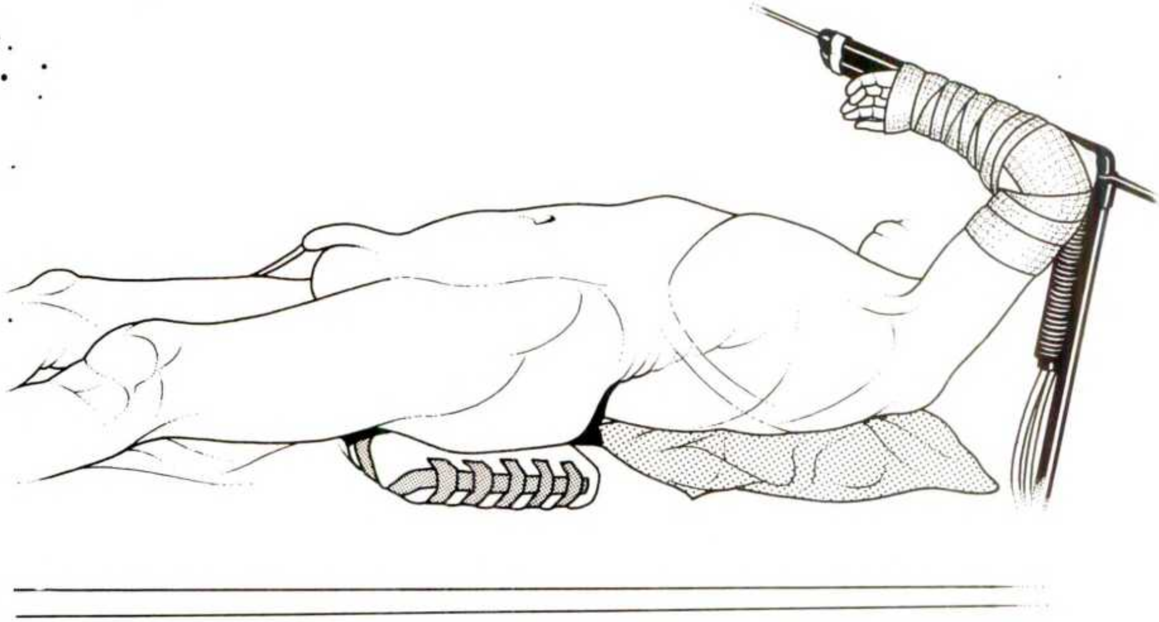


Fig. 1. Position of patient for extraperitoneal exposure.

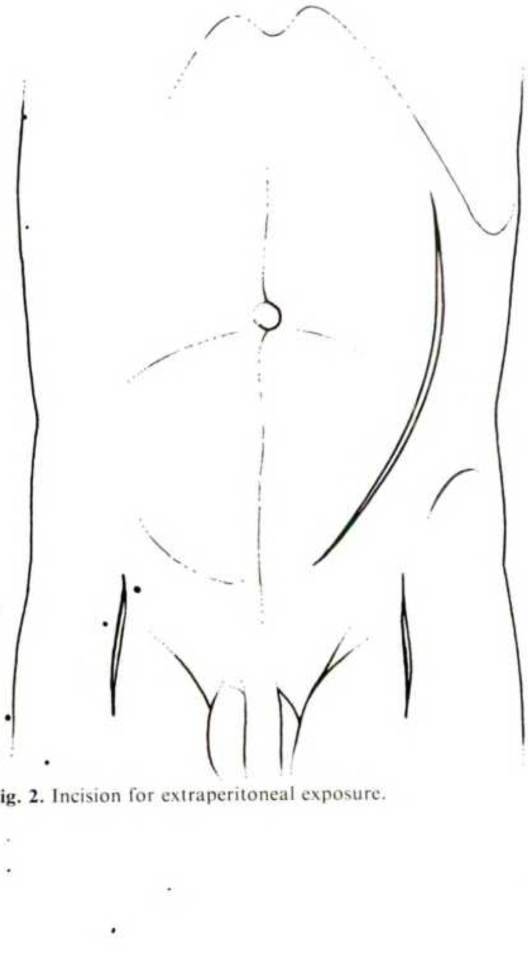


Fig. 2. Incision for extraperitoneal exposure.

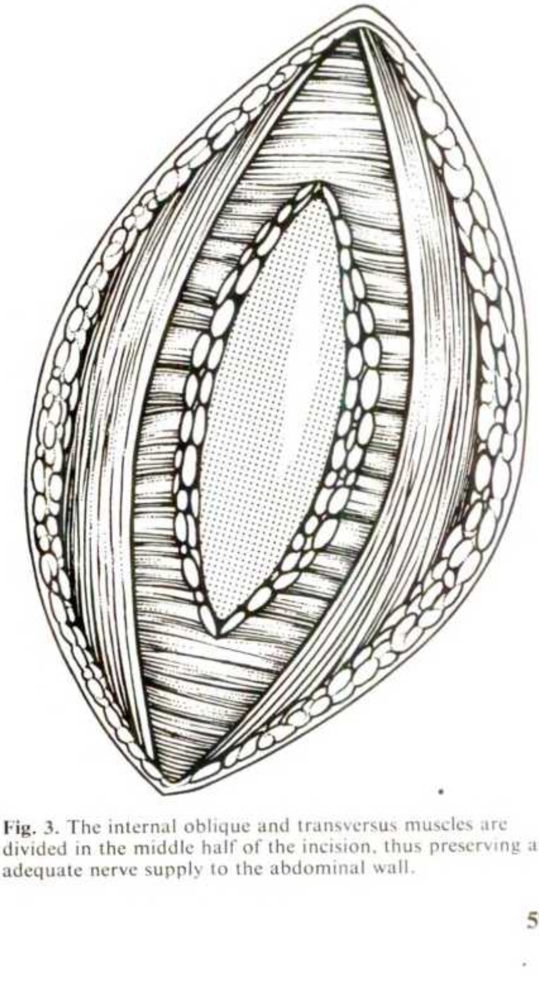


Fig. 3. The internal oblique and transversus muscles are divided in the middle half of the incision, thus preserving an adequate nerve supply to the abdominal wall.

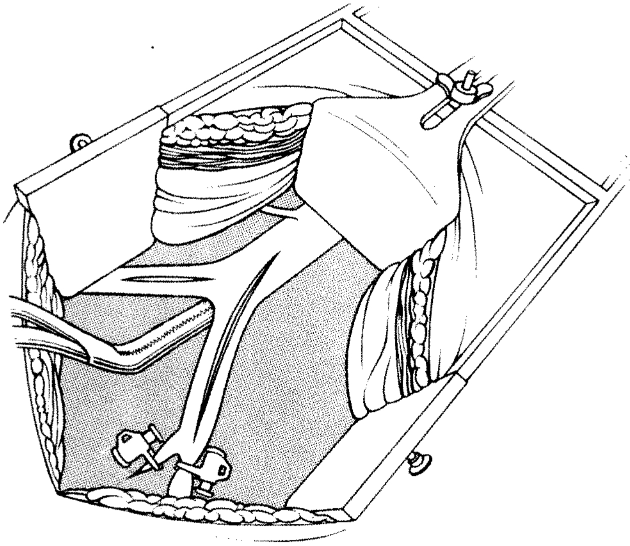


Fig. 4. Exposure of lower abdominal aorta and common iliac arteries.

few hours preoperatively and continued for 4 days. Originally heparin was given intraoperatively, but for the past 2 years a single loading dose of 10 000 units is injected intravenously before the induction of anaesthesia. Since the introduction of this latter method there has been no clinical evidence of pulmonary embolism, and indeed no clinical evidence of major deep venous thrombosis in the lower limb following aorto-iliac reconstruction.

For the extraperitoneal exposure certain points need emphasis. The left side of the patient must be tilted slightly upwards on sandbags and the ipsilateral arm supported (*Fig*. 1). Our incision differs somewhat from that described by Rob (1963) and resembles that of Rutherford Morrison. The skin incision is sickle-shaped with the upper end curving medially to the costal margin (*Fig*. 2). The external oblique muscle and aponeurosis is split along the line of its fibres. The underlying internal oblique and transversus muscles are then divided with diathermy in the middle half of the incision. The fibres in the upper and lower quarters of the incision are not divided, and this seems to preserve an adequate nerve supply to the abdominal wall (*Fig*. 3). The rectus muscle is not divided. The use of a Goligher self-retaining retractor is absolutely essential and overcomes the problem of retraction to which Rob (1963) refers in his paper. The instrument has been modified by us to provide different depths of blade, and it is no exaggeration to say that it saves one assistant—an important factor in many hospitals where skilled assistance is not always readily available. Abdominal packs are not required, only a small dab, with radio-opaque strip, being placed behind each blade of the retractor (*Fig*. 4). The abdominal incision is closed with a split tube drain. Redivac drains are used for groin incisions. It is quite possible through this incision to obtain an adequate exposure for disobliteration of the abdominal aorta and both common iliac arteries or, alternatively, for transection of the aorta, proximal disobliteration and end-to-end attachment of a bifurcation graft. Small aneurysms have also been resected through this approach. The distal graft anastomosis is performed in the groin, end to side, to the common femoral artery opposite the origin of the profunda femoris artery. When a bypass graft is inserted local common femoral disobliteration is often performed, and occasionally some type of profundaplasty. Left lumbar sympathectomy was performed concomitantly in the majority of operations by coagulation of the lower lumbar ganglia with diathermy. Postoperatively each patient received 500 ml of low molecular weight dextran (Rheomacrodex) daily for the first 3 days.

Postoperative care is in the general surgical ward and is the routine for any abdominal operation. No patient in the extraperitoneal group has required treatment in an intensive therapy unit. Anticoagulants are not used postoperatively. Because the peritoneum is not opened, convalescence is remarkably easy. A nasogastric tube is usually inserted by the anaesthetist during the operation, and in the majority of cases is removed 24 hours later. Limited oral fluids are commenced on the first postoperative day, and are increased with the onset of intestinal activity. The length of stay in hospital after surgery has been shortened by 2 or 3 days but it is our practice to keep the patient in hospital until the twelfth day when the skin sutures are removed. Patients are much more mobile in the early postoperative period and discomfort is little more than that experienced after herniorrhaphy or appendicectomy.

Results

Two hundred and three patients were followed up for this report, 90 having undergone the extraperitoneal operation and 113 being operated on by the transperitoneal approach. One hundred and twenty-five patients (62 per cent) presented with intermittent claudication and the remaining 78 (38 per cent) with severe rest pain or established gangrene. Most of the latter patients had superficial femoral occlusions in addition to their aorto-iliac disease. Severe hypertension was uncommon but some elevation of the diastolic pressure was found in one-third of the patients. Electrocardiographic evidence of coronary artery disease was noted in 25 per cent of all the patients. More than a quarter of the patients were aged over 60 years.

Operative mortality

Seven patients died within 1 month of operation, a mortality rate of 3·5 per cent. Five of the 7 patients had presented with rest pain or gangrene. Three deaths occurred in the extraperitoneal group (90 patients) and 4 in the transperitoneal group (103 patients). The causes of the deaths were: pulmonary embolism 2, cerebrovascular accident 2, coronary thrombosis 1, bronchopneumonia 1, haemorrhage into duodenum 1.

Late postoperative deaths

Forty-three patients (20 per cent) died at intervals between 3 months and 9 years postoperatively, 13 of these having survived for 5 years. Twenty-four (56 per cent) were certified as having died from coronary thrombosis and 5 from a cerebrovascular accident. In 22 of these 43 patients the grafts were patent at the time of death. The low patency rate in this group may well relate to the fact that 32, or three-quarters, of the late deaths were in patients who presented with rest pain or gangrene and had more extensive disease.

Reoperation

Early reoperation was performed on 7 patients in the claudication group in whom re-thrombosis had occurred. Three patients had been treated by the extraperitoneal approach and 4 by the transperitoneal approach. Four were successfully treated by thrombectomy and 3 by some further reconstruction. Late reoperation was performed on 15 patients—8 from the extraperitoneal group and 7 from the transperitoneal group. The operations done were 6 axillofemoral grafts (all of which have subsequently thrombosed), 2 excisions of false aneurysms, 1 thrombectomy and replacement of one limb of a bifurcation graft in 6 patients.

Postoperative complications

The postoperative complications are set out in *Table I*. It will be seen that complications were twice as frequent in the transperitoneal group as in the extraperitoneal group. There have been no haematomas in the groin since Redivac drains have been used. The table cannot convey the much smoother convalescence of patients who have been treated by the extraperitoneal approach.

Table I: POSTOPERATIVE COMPLICATIONS

Complications	Extra-peritoneal group (90 patients)	Trans-peritoneal group (113 patients)	Total (203 patients)
Bronchopneumonia	1	3	4
Coronary thrombosis	1	2	3
Cerebrovascular accident	—	2	2
Deep vein thrombosis (symptomatic)	3	7	10
Pulmonary embolus (symptomatic)	2	5	7
Haemorrhage into duodenum	—	1	1
Paralytic ileus	—	2	2
Wound dehiscence	—	1	1
Retroperitoneal haemorrhage	1	—	1
Incisional hernia	—	3	3
Minor wound sepsis	3	2	5
Haematoma in groin	4	—	4
Femoral aneurysm	—	1	1
False femoral aneurysm	—	2	2
Neuralgic pain	—	2	2
Total	15	33	48

Follow-up

Of the 78 patients presenting with rest pain or gangrene, 24 (30 per cent) came to amputation. Forty-six patients were alive and 35 (86 per cent) of them had relief of symptoms for a year or more, 13 being symptom-free at 4 years and 6 for over 7 years. It seems satisfactory to note that 70 per cent of the painful legs were saved from amputation.

Of the 125 patients presenting with claudication, 13 had died. Only 3 patients lost a limb—2 at 2 years and 1 at 7 years after operation. We decided to report only the results of the 69 patients who had undergone surgery at least 4 years previously. In 62 (89 per cent) of these the reconstructions had remained patent (4 for 13 years, and 12 for over 7 years). However, only 42 patients (61 per cent) were totally symptom-free. The remaining 20 patients (28 per cent) were significantly improved in that some calf claudication was experienced but only after walking fairly long distances. We submit, therefore, that patency rates alone may not indicate complete success of a surgical procedure. The results, not surprisingly, were better in the patients whose disease was mainly confined to the aorto-iliac segment.

Discussion

These results are comparable with those in other series and satisfy us that aorto-iliac reconstruction for atherosclerosis is a worthwhile procedure, bearing in mind that one is dealing with only a part of a generalized, progressive and frequently lethal disease. Certainly the operation, in our hands, is more worthwhile than femoropopliteal grafting procedures. We could find no significant difference in the long term results following the two types of operative exposure. However, both junior doctors and nursing staff agree that the postoperative convalescence of those treated by the extraperitoneal approach is noticeably smoother and easier. Operating time is significantly shortened by this approach, both the exposure and the closure being considerably quicker. This, for us, is an important consideration since these operations were done as part of a normal general operating list.

References

DOUGLAS D. (1973) The ischaemic limb. *J. R. Coll. Surg. Edinb.* **18**, 259–274.

GASPARD D. J., COHEN J. L. and GASPAR M. R. (1972) Aorto-ilio femoral thromboendarterectomy vs. bypass graft. *Arch. Surg.* **105**, 898–901.

INAHARA T. (1972) Endarterectomy for occlusive disease of the aorto-iliac and common femoral arteries. *Am. J. Surg.* **124**, 235–243.

IRVINE W. T., BOOTH R. A. D. and MYERS K. (1972) Arterial surgery for aorto-iliac occlusive vascular disease. Early and late results in 238 patients. *Lancet* **1**, 738–741.

MARTIN P. and MARSTON J. A. P. (1973) Peripheral vascular disease. In: TAYLOR S. (ed.) *Recent Advances in Surgery*. Edinburgh, Churchill Livingstone, pp. 404–405.

MOZERSKY D. J., SUMNER D. S. and STRANDNESS D. E. (1972) Long term results of reconstructive aorto-iliac surgery. *Am. J. Surg.* **123**, 503–509.

PILCHER D. B., BARKER W. F. and CANNON J. A. (1970) An aorto-iliac endarterectomy case series followed 10 years or more. *Surgery* **67**, 5–17.

ROB C. G. (1963) Extraperitoneal approach to the abdominal aorta. *Surgery* **53**, 87–89.

STIPA S. and SHAW R. S. (1968) Aorto-iliac reconstruction through a retro-peritoneal approach. *J. Cardiovasc. Surg.* **14**, 224–236.

TAYLOR G. W. (1973) Chronic arterial occlusion. In: BIRNSTINGL M. (ed.) *Peripheral Vascular Surgery*, London, Heinemann, pp. 211–234.

VAN LENT D., KUIJPERS P. J., SKOTNICKI S. H. and MEYER I. (1974) Aorto-iliac surgery: a comparative study between thromboendarterectomy and bypass. *J. Cardiovasc. Surg.* **15**, 352–355.

WATT J. K., GILLESPIE G., POLLACK J. G. and REID W. (1974) Arterial surgery in intermittent claudication. *Br. Med. J.* **1**, 23–26.

Br. J. Surg. Vol. 62 (1975) 601–604

Oesophagogastrostomy without a drainage procedure in oesophageal carcinoma

I. B. ANGORN*

SUMMARY

Ten patients with carcinoma of the lower third of the oesophagus who had oesophagogastrectomy followed by oesophagogastrostomy without a drainage procedure were investigated 6 months postoperatively. Postoperative symptomatic evaluation and modified Visick grading of the results were carried out by an independent observer. Objective assessment included fibre-optic endoscopy of the oesophagus, stomach and duodenum, gastric acid secretory studies and measurement of gastric emptying times following the ingestion of a barium food mixture.

Eight of the 10 patients had an excellent or very good result and the remaining 2 were graded as satisfactory. No evidence of macroscopic oesophagitis or gastritis was detected and pyloric obstruction was never observed. Gastric emptying time was not prolonged. The results obtained support the concept that a drainage procedure is unnecessary after oesophagogastrostomy.

IT has been generally accepted that oesophagogastrectomy followed by oesophagogastrostomy must be accompanied by a pyloroplasty, because of the incidental vagotomy and resulting gastric stasis. The Heineke–Mikulicz pyloroplasty has been the procedure of choice, but some surgeons perform Ramstedt pyloromyotomy or dilatation of the pylorus as an alternative. Reports exist of clinical series where oesophagogastrostomy has been performed without a drainage procedure (Logan, 1963; Zacho and Fischermann, 1965; Collis, 1971). The majority of these patients have shown no untoward sequelae. Shapiro et al. (1972) reported an experimental study on mongrel dogs and concluded that a drainage procedure is unnecessary after oesophagogastrostomy. Little information is available on the behaviour in humans of the gastric remnant following oesophagogastrostomy without drainage. The present study reports the results obtained from investigating patients in whom the pylorus was left inviolate after oesophagogastrostomy.

Patients and methods

During the period January 1972 to July 1973, 20 patients suffering from carcinoma of the lower third of the oesophagus were submitted to oesophagogastrectomy followed by oesophagogastrostomy without a drainage procedure. A two-phase technique similar to the Ivor Lewis (1946) procedure was employed. Ten of these patients (8 males and 2 females) were evaluated at 6 months after operation.

Symptomatic evaluation

An independent observer ascertained the patients' ability to eat and swallow normally, and inquired for the presence of symptoms which might be referable to the operative procedure. These were: dysphagia, anorexia, nausea, fullness, heartburn, regurgitation, pyrosis, flatulence, dumping, diarrhoea, vomiting. A modified Visick (1948) grading of the results was carried out. Four categories of result are recognized (*Table I*). From a practical point of view categories I and II can be regarded as highly satisfactory.

Table I: GRADING OF RESULTS (MODIFIED VISICK CLASSIFICATION)

Category	Definition
I Excellent	Symptom-free
II Very good	Mild symptoms, but patient considers result perfect
III Satisfactory	Mild or moderate symptoms not controlled by care, but not interfering with work or enjoyment of life. Patient and surgeon satisfied
IV Unsatisfactory	Moderate or severe symptoms compromising work and enjoyment of life. Patient or doctor dissatisfied with result

Endoscopic examination

The oesophagus, stomach and duodenum were examined using the long (120-cm) Olympus GIF end-viewing fibre-optic duodenoscope. The oesophagus was examined for overt reflux and the presence of macroscopic oesophagitis. Oesophagitis was defined and graded according to the criteria of Skinner and Belsey (1967). They defined four categories: grade I, mucosal redness; grade II, isolated scattered superficial ulceration: grade III, chronic ulcer with infiltration and thickening deep to the ulcer; grade IV, stricture. The oesophageal mucosa was biopsied immediately above the anastomotic site.

The stomach was examined to determine the presence of gastritis. Criteria for the diagnosis of gastritis were: mucosal oedema, hyperaemia, excess adherent mucus, petechial or confluent mucosal haemorrhages, erosions and superficial ulcers. The behaviour of the pylorus was observed visually and the nature of gastric peristalsis noted.

Gastric acid studies

Gastric acid output was measured by the method of Kay (1967), except that 6 μg/kg intramuscular pentagastrin were used as a stimulus.

---

* Department of Surgery, University of Natal, Durban, South Africa.

Table II: POSTOPERATIVE SYMPTOMS

Symptom	No. of cases	% of total
Dysphagia	0	0
Anorexia	0	0
Nausea	0	0
Fullness	2	20
Heartburn	0	0
Regurgitation	1	10
Pyrosis	0	0
Flatulence	0	0
Vomiting	0	0
Dumping	0	0
Diarrhoea	2	20

Table III: MODIFIED VISICK GRADING OF RESULTS

Category	No. of cases	% of total
I Excellent	5	50
II Very good	3	30
III Satisfactory	2	20
IV Unsatisfacory	0	0

Table IV: POSTOPERATIVE GASTRIC ACID STUDIES

	BAO	MAO
Number	10	10
Mean	0·25 mEq/h	2·2 mEq/h
s.d.	0·34	1·4
s.e.	0·10	0·44

BAO, Basal acid output. MAO, Maximal acid output.

Gastric emptying time

This was studied in all 10 patients and compared with normal control subjects and patients who had undergone truncal vagotomy and pyloroplasty for duodenal ulcer who were matched according to age and sex. After an overnight fast a plain X-ray film of the abdomen was taken. Then a semi-fluid meal consisting of 200 ml porridge, 30 ml milk, 30 ml barium suspension and 2 teaspoonfuls of sugar was served warm to all the patients. It was eaten using a spoon with the patient sitting upright in a chair and consumed in 5–10 minutes. Further abdominal X-rays were taken at 15, 30, 120, 180 and 240 minutes with the patient lying in the prone position. In the intervals between exposures the patient was free to sit or walk around the X-ray department. The films were assessed at 15 minutes to detect commencement of gastric emptying and thereafter to ascertain when the stomach was completely empty.

Results

Symptomatic evaluation

The incidence of postoperative symptoms is given in *Table II*. Five of the 10 patients were completely symptom-free. The 2 patients complaining of fullness were able to control this symptom by taking smaller and more frequent meals. They both maintained their weight and considered the result of operation as gratifying. One patient suffered from regurgitation when in the recumbent position, but this was easily controlled by elevating the head end of the bed on two bricks. Two patients both with achlorhydria passed three to five loose yellow stools per day. This symptom was episodic and could be controlled by the administration of tetracycline 1 g daily in divided doses for a period of 3 weeks. *Table III* indicates the overall functional results using a slight modification of the Visick (1948) classification. Eight of the 10 patients (80 per cent) showed an excellent or very good result. The 2 patients in grade III category were in no way compromised by their symptoms.

Endoscopic examination

All 10 patients revealed a healthy distal oesophagus with no evidence of macroscopic oesophagitis. Oesophageal biopsy at the anastomotic site demonstrated microscopic evidence of chronic inflammatory changes in 3 patients. One of these patients complained of regurgitation.

No macroscopic evidence of gastritis was present in any of the patients and reflux of duodenal contents was not observed. The pylorus remained open and patulous a greater percentage of time than normal but was capable of closing spontaneously. Both tonic contraction of the stomach and peristaltic waves occurred during the course of the examination. Antiperistalsis was observed infrequently.

Gastric acid studies

The results of basal acid output (BAO) and maximal acid output (MAO) are summarized in *Table IV*. Two of the 10 patients had absolute achlorhydria and the highest maximal acid output was 5 mEq/h.

Gastric emptying time

Gastric emptying had begun by the time the 15-minute film was exposed in all the patients who had undergone truncal vagotomy and pyloroplasty, but in only 6 of the 10 control subjects and 7 of the 10 patients after oesophagogastrostomy (*Fig*. 1). These differences are not statistically significant.

All the patients who had undergone oesophagogastrostomy and all those who had undergone truncal vagotomy and pyloroplasty showed complete emptying of the stomach at 4 hours. The stomach was completely empty in 7 of the 10 control subjects (*Fig*. 2). These differences are not statistically significant.

Discussion

Following oesophagogastrectomy for carcinoma of the lower third of the oesophagus, alimentary tract continuity is ideally restored by oesophagogastrostomy (Hanna et al., 1967). This procedure has generally been complemented by pyloroplasty because of the incidental vagotomy that is performed. Little evidence exists that pyloroplasty is necessary, and evaluation of our patients indicates that it can safely be omitted.

Symptomatic evaluation by an independent observer 6 months postoperatively revealed that 8 out of 10 patients had a highly satisfactory result. Two out of the 10 patients suffered from diarrhoea (three to five loose yellow stools per day) and weight gain was slow. Both returned to full employment. In all the patients the prime objective of surgery for oesophageal carcinoma, viz. ability to swallow and eat comfortably, was achieved.

Fibre-optic endoscopy of the oesophagus revealed no evidence of macroscopic oesophagitis, but 3 patients, one of whom suffered from regurgitation when recumbent, revealed microscopic changes suggestive of oesophagitis. Allison (1970) stated that oesophagitis may be due to reflux of acid gastric secretions or alkaline duodenal contents. He emphasized that no close correlation exists between the degree of reflux and the frequency and degree of oesophagitis, and that mucosal susceptibility may be a contributing factor. In the present series the absence of symptoms and objective evidence of oesophagitis may be due to three factors. These are: gravity emptying of acid gastric juice, the presence of an intact pylorus preventing duodenal reflux and hypochlorhydria or achlorhydria. It has also been suggested that valvular techniques of oesophagogastric reconstruction may prevent symptomatic reflux (Pearson et al., 1969).

Examination of the stomach revealed no evidence of macroscopic gastritis. The pylorus appeared patulous and remained open a greater percentage of time than normal, but its ability to contract and close spontaneously was still present. Pyloric spasm was never observed. Poorly synchronized peristaltic waves were seen; also infrequent antiperistaltic waves proceeding from the antrum proximally. This desynchronization, as well as diminution in amplitude and duration of peristaltic activity in the vagotomized stomach, has been likened to cardiac atrial fibrillation in slow motion by Nelsen et al. (1967).

Gastric emptying of a food/barium meal measured radiographically is a relatively crude technique. Despite this, two definite observations can be made. The start of gastric emptying can be seen and the time taken for the stomach to empty completely can be ascertained. There was no delay in commencement of gastric emptying in patients following oesophagogastrostomy without pyloroplasty and no prolongation of the complete emptying time. A gastric drainage procedure to prevent gastric stasis is unnecessary, and a high oesophagogastric anastomosis when combined with a drainage procedure has been shown to result uniformly in dumping symptoms (Hanna et al., 1967).

Vagotomy may cause unsynchronized peristaltic waves, not coordinated in time or direction of propagation, resulting in impaired orthograde propulsion of food content (Nelsen et al., 1967). The absence of gastric stasis following oesophagogastrectomy and endothoracic oesophagogastrostomy can be due to various factors. The open or patulous pylorus offers no resistance to gastric emptying. The vertical position of the gastric remnant in the chest allows gravity emptying. Reduction in size of the stomach permits easier filling to capacity, and the full stomach empties at a more rapid rate than the partially filled one due to an increase in mural tension (Hunt, 1959).

Conclusion

Postoperative symptomatic evaluation, endoscopic examination, gastric acid analysis and studies of gastric emptying time in patients who have undergone oesophagogastrostomy without pyloroplasty following oesophagogastrectomy support the concept that a drainage procedure is unnecessary after this anastomosis.

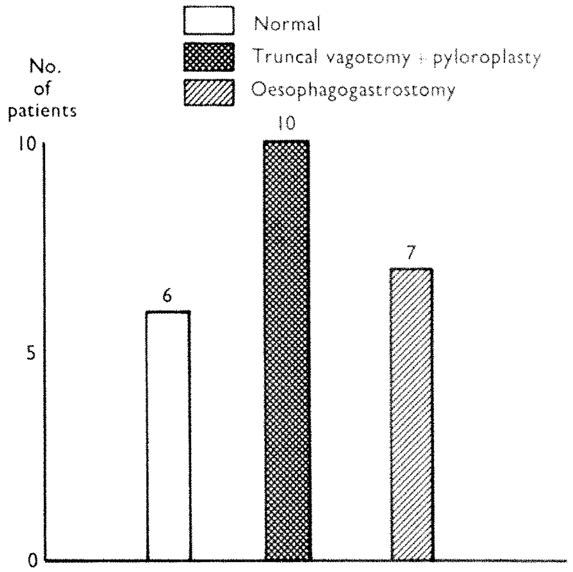


Fig. 1. Food/barium mixture in duodenum at 15 minutes.

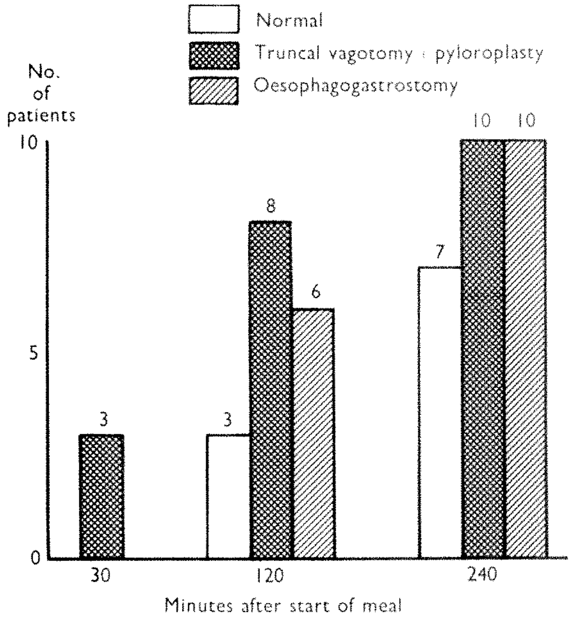


Fig. 2. Time required for stomach emptying.

Acknowledgements

This study was carried out with financial support from Keatings Pharmaceuticals Ltd. Thanks are due to Mrs B. Slater for typing the manuscript.

References

ALLISON P. R. (1970) Peptic oesophagitis and oesophageal stricture. *Lancet* **2**, 199–201.

COLLIS J. L. (1971) Surgical treatment of carcinoma of the oesophagus and cardia. *Br. J. Surg.* **58**, 801–804.

HANNA E. D., HARRISON A. W. and DERRICK J. R. (1967) Long-term results of visceral esophageal substitutes. *Ann. Thorac. Surg.* **3**, 111–117.

HUNT J. N. (1959) Gastric emptying and secretion in man. *Physiol. Rev.* **39**, 491–533.

KAY A. W. (1967) An evaluation of gastric acid secretion tests. *Gastroenterology* **53**, 834–843.

LEWIS I. (1946) The surgical treatment of carcinoma of the oesophagus. *Br. J. Surg.* **34**, 18–31.

LOGAN A. (1963) The surgical treatment of carcinoma of the esophagus and cardia. *J. Thorac. Cardiovasc. Surg.* **46**, 150–161.

NELSEN T. S., EIGENBRODT E. H., KEOSHIAN C. B. and JOHNSON L. (1967) Alterations in muscular and electrical activity of the stomach following vagotomy. *Arch. Surg.* **94**, 821–835.

PEARSON F. G., HENDERSON R. D. and PARRISH R. M. (1969) An operative technique for the control of reflux following oesophagogastrostomy. *J. Thorac. Cardiovasc. Surg.* **58**, 668–673.

SHAPIRO S., HAMLIN D. and MORGENSTERN L. (1972) The fate of the pylorus in esophagoantrostomy. *Surg. Gynecol. Obstet.* **135**, 216–218.

SKINNER D. B. and BELSEY R. H. R. (1967) Surgical management of oesophageal reflux and hiatus hernia. *J. Thorac. Cardiovasc. Surg.* **53**, 33–54.

VISICK A. H. (1948) A study of failures after gastrectomy. *Ann. R. Coll. Surg. Engl.* **3**, 266–284.

ZACHO A. and FISCHERMANN K. (1965) Surgical treatment of malignancies of the oesophago-gastric junction. *Acta Chir. Scand.* (*Suppl.* 356), 121–129.

Br. J. Surg. Vol. 62 (1975) 605–607

Antrectomy with Roux-en-Y anastomosis in the treatment of peptic oesophagitis with stricture

C. M. S. ROYSTON, B. L. DOWLING AND J. SPENCER*

SUMMARY

A series of 8 patients with severe oesophageal strictures secondary to reflux oesophagitis who have been treated by antrectomy with Roux-en-Y anastomosis is described. There was 1 postoperative death. The remaining patients have been completely relieved of heartburn and all have had a dramatic improvement in their dysphagia. This method of treatment is strongly recommended for patients who have had prior surgery to the hiatus which has failed, and for those who are too elderly or frail to withstand a direct attack on their oesophageal stricture.

REFLUX oesophagitis with stricture formation occurring after previous surgery on the diaphragmatic hiatus presents a difficult surgical problem. A second operation on the hiatus is often a complicated and hazardous procedure, particularly in the elderly, and results are frequently disappointing.

In recent years increasing evidence has accumulated that biliary and pancreatic secretions may be partly responsible for the mucosal damage in reflux oesophagitis. Oesophagojejunostomy after total gastrectomy is often complicated by oesophagitis if a loop of jejunum is used; it was for this reason that the use of a Roux loop was adopted (Kelly et al., 1954; Helsingen, 1960).

Experimental evidence for bile as a causative factor has come from the rhesus monkey studies of Gillison et al. (1972), whilst Lambert's (1962) investigations in the rat have suggested that pancreatic juice may be more important.

Wangenstein and Levin (1949) were the first to observe that reflux oesophagitis could be improved by operations on the stomach. Holt and Large (1961) were the first to employ a Roux-en-Y diversion in the primary treatment of peptic strictures of the oesophagus. They performed this in conjunction with resection of the stricture or extensive resection of the stomach in the majority of their patients. All showed marked improvement in their oesophagitis.

This is a report of a follow-up study of 8 patients with severe strictures of the oesophagus secondary to oesophagitis who have been treated with a limited antrectomy and Roux-en-Y jejunogastric anastomosis without resection of the oesophageal stricture.

Clinical material

The present series consists of 8 patients (mean age 61 years) with severe stricture secondary to reflux oesophagitis. Dysphagia and heartburn were the predominant symptoms in all the patients, 6 of whom had had at least one previous operation on the hiatus.

All the patients first had their strictures dilated with Eder–Puestow dilators (Puestow, 1955), either a few days before operation or on the operating table immediately before the diversion.

Table I summarizes the case histories. The 6 patients who had undergone previous surgery to the hiatus were treated by a limited antrectomy with Roux-en-Y reconstruction (*Fig.* 1). The Roux limb was constructed so that it was at least 45 cm long. In the 2 patients who had not had previous surgery a truncal vagotomy was added as well.

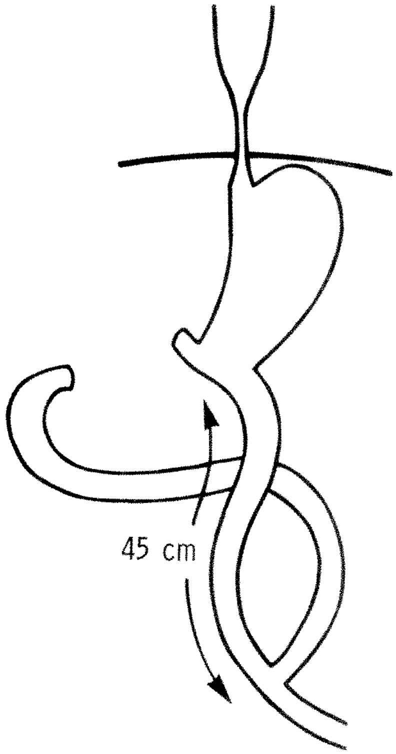


Fig. 1. Diagrammatic representation of the Roux-en-Y diversion procedure.

The following is a typical case history:

E. B., a female aged 70. Symptoms of heartburn started in 1964; these gradually progressed and in 1969 she developed dysphagia to solids. A barium meal examination at this time showed a small sliding hiatus hernia with a stricture at the lower end. Conservative treatment afforded little improvement, so in February 1972 a thoraco-abdominal Collis repair (Collis, 1972) of the hiatus hernia was performed. After this, the patient's dysphagia improved but she continued to suffer from heartburn. In September 1973 dysphagia returned and was rapidly progressive until she could swallow only small volumes of liquid. A barium swallow study (*Fig. 2a*) performed at this time revealed a very tight stricture of the oesophagus, which was confirmed on endoscopy. Marked oesophagitis was present. Initial treatment was conservative, her stricture being dilated with Eder–Puestow dilators. These measures gave temporary relief and in May 1974 an antrectomy with Roux-en-Y diversion was performed. Postoperatively her pain disappeared and her dysphagia rapidly improved, until at 6 weeks she could eat anything. No further dilatations have been necessary. She has now been followed up for 15 months, has gained 12·7 kg in weight and is entirely asymptomatic. *Fig. 2b* shows a barium swallow film 6 months after operation.

---

* Northampton General and Hammersmith Hospitals, London.

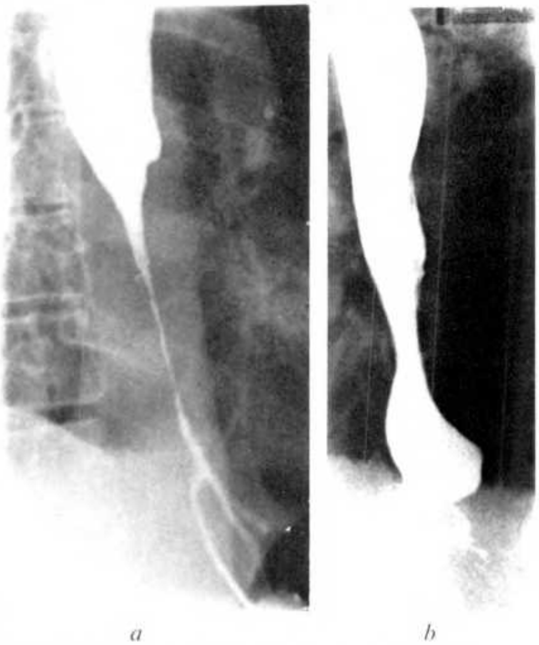


Fig. 2. E. B. Barium swallow films (*a*) before and (*b*) 6 months after the Roux-en-Y procedure.

Results

The follow-up period ranges from 11 to 20 months. One patient who was 74 and very weak and frail before operation died during the postoperative period. Despite intravenous feeding and oesophageal dilatations he remained weak and developed a fulminating bronchopneumonia on the tenth postoperative day. The remaining 7 patients all had complete relief of heartburn after operation. Two were cured of dysphagia without further dilatations. Another 3 were cured after a single dilatation, and 1 patient was dilated twice and is now asymptomatic. The final patient who had a very long history of dysphagia and had been performing self-bouginage for many years has had marked improvement, and can use a larger size bougie at less frequent intervals. He is still improving.

Discussion

Reflux of acid was thought to be the cause of oesophagitis. Recently, however, increasing evidence has accumulated that biliary and pancreatic secretions may be partly responsible for the mucosal damage in reflux oesophagitis. Experimental evidence for bile as a causative factor has come from the rhesus monkey studies of Gillison et al. (1972), who found that reflux of bile and acid caused severe oesophagitis, whereas reflux of acid alone had little effect. Lambert (1962), performing diversionary experiments in Wistar rats, found that pancreatic secretion produced a more

Table I: DETAILS OF THE PRESENT SERIES

Case	Age	Length of history (yr)	Previous surgery	Preoperative state	Result	Follow-up period (mth)
A. W.	68	4	Nil	Oesophagitis + +. Stricture. Dysphagia. Liquids only. Variable	Eats anything. No dilatation. No pain	20
J. S.	56	6	Nissen repair in July 1973. Symptoms recurred 1 mth later	Oesophagitis + +. Stricture 40 cm. Fluids only	Eats anything. No pain. Dilated postoperatively × 1	20
A. W.	61	14	Allison repair in Aug. 1965. Nissen repair Nov. 1973. Symptoms recurred 3 mth later	Oesophagitis + +. Stricture 30 cm. Semi-solids only	Eats anything. Dilated postoperatively × 2	11
I. D.	48	15	Collis repair in Feb. 1970. Oesophagogastroplexy in April 1970	Regurgitation + +. Dysphagia to solids. Heartburn	Eats anything. Postcibal fullness. Dilatation × 1	13
U. C.	63	13	Allison repair in May 1963. Has since suffered heartburn and recent dysphagia	Dysphagia to solids. Heartburn + +. Stricture 35 cm	Eats anything. No pain. No dilatation	11
E. B.	70	7	Collis repair in Feb. 1972. Heartburn persisted. Dysphagia at 7 mth	Dysphagia. Fluids only. Heartburn + +. Stricture 30 cm	Eats anything. Weight increase. Dilated × 1	15
R. W.	53	50*	Oesophageal perforation repaired in 1963. Allison repair in Mar. 1966	Dysphagia. Fluids only. Heartburn + +. Tight stricture 37 cm	Eats anything. Diarrhoea —mild. Weight increase. Self-bouginage	12
W. H.	74	½	Nil	Dysphagia + +. Small volume of fluid only. Heartburn +	Died postoperatively. Bronchopneumonia	

* Began at 2½ years of age.

marked oesophagitis than biliary secretions, but the combination of biliary and pancreatic secretions caused the more severe oesophageal changes. Studies in man by Gillison et al. (1969) have shown that the symptom of heartburn is associated with reflux of duodenal contents into the stomach and oesophagus. Crumplin et al. (1974) investigated bile salts in the stomach of patients with symptomatic hiatus hernia and of control subjects. They found an increased incidence of bile salts in the stomach following a meal in patients with hiatus hernia, but there was no single constituent of the bile that was more prevalent.

Wangenstein and Levin (1949) were the first to observe that oesophagitis could be improved by operations on the stomach. They reported 6 patients with severe oesophagitis and stricture of the lower oesophagus who after high subtotal Polya gastrectomy showed a marked improvement in their symptoms. Similarly, Tanner and Westerholm (1968) reported a series of 22 patients who underwent a modified Balfour gastrectomy for peptic stricture of the lower oesophagus; all had marked improvement in their symptoms. Cenni et al. (1966) described 3 patients who developed severe oesophagitis following Polya gastrectomy. All were relieved of their symptoms by Roux-en-Y conversion.

Holt and Large (1961) were the first to employ a Roux-en-Y diversion in the primary treatment of peptic strictures. They reported 10 cases of stricture that were treated by distal gastrectomy with Roux-en-Y jejunogastric anastomosis. In 4 of the patients the stricture had occurred following a Grondahl procedure for achalasia. Four of the 10 cases also had a resection of the stricture, and 9 out of 10 had an extensive resection of the stomach. All showed marked improvement in their oesophagitis. Weaver et al. (1970) have recently reported the 8–17-year follow-up of these patients, in all of whom the improvement has been maintained. Payne (1970) reported a series of 15 patients with severe oesophagitis, 13 of whom had a hemigastrectomy with Roux-en-Y diversion performed. Six of these patients had a severe stricture of the oesophagus which was resected; all showed marked improvement.

In the series reviewed, when Roux-en-Y diversion was used for the treatment of oesophageal strictures it was in most cases performed in combination with either resection of the stricture or very extensive subtotal gastrectomy. In our series dramatic improvement in the severity of the dysphagia occurred despite the presence of an apparently tight fibrous stricture. The most striking feature in our series was the complete relief of heartburn; none of the patients had any heartburn from the day of operation onwards. The improvement in the dysphagia was much slower, often taking 2–3 months before marked improvement occurred. This latter observation was confirmed on endoscopy. In the patients undergoing endoscopy soon after operation little change was apparent; however, after 3 months mucosal appearances had returned to normal.

Acknowledgements

We wish to thank the Department of Medical Illustration of the Royal Postgraduate Medical School for the figures and Mrs Hilary Hart for typing the manuscript.

References

CENNI L. J., COX W. F. and HANDS S. (1966) Gastric surgery. The Roux-en-Y procedure for bile oesophagitis. *J. Kans. M. Soc.* **67**, 421.

COLLIS J. L. (1972) Treatment of reducible hiatus hernia of the sliding type. *Proc. R. Soc. Med.* **65**, 35–37.

CRUMPLIN M. K. H., STOL D. W., MURPHY G. M. and COLLIS J. L. (1974) The pattern of bile salt reflux and acid secretion in sliding hiatus hernia. *Br. J. Surg.* **61**, 611–616.

GILLISON E. W., CAPPER W. M., AIRTH G. R., GIBSON M. J. and BRADFORD I. (1969) Hiatus hernia and heartburn. *Gut* **10**, 609–613.

GILLISON E. W., KUSAKARI K, BOMBECK C. T. and NYHUS L. M. (1972) The importance of bile in reflux oesophagitis and the success in its prevention by surgical means. *Br. J. Surg.* **59**, 794–798.

HELSINGEN N. (1960) Oesophagitis following total gastrectomy. *Acta Chir. Scand.* **118**, 190–201.

HOLT C. J. and LARGE A. M. (1961) Surgical management of reflux oesophagitis. *Am Surg.* **153**, 555–562.

KELLY W. D., MACLEAN L. D., PERRY J. F. and WANGENSTEIN O. H. (1954) A study of patients following total and near-total gastrectomy. *Surgery* **35**, 964–982.

LAMBERT R. (1962) Relative importance of biliary and pancreatic secretions in the genesis of oesophagitis in rats. *Am. J. Dis.* **7**, 1026–1033.

PAYNE W. S. (1970) Surgical treatment of reflux oesophagitis and stricture associated with permanent incompetence of the cardia. *Mayo Clin. Proc.* **45**, 553–562.

PUESTOW K. L. (1955) Conservative treatment of stenosing diseases of the oesophagus. *Postgrad. Med.* **18**, 6–14.

TANNER N. C. and WESTERHOLM P. (1968) Partial gastrectomy in the treatment of oesophageal stricture after hiatus hernia. *Am. J. Surg.* **115**, 449–453.

WANGENSTEIN O. H. and LEVIN N. L. (1949) Gastric resection for oesophagitis and stricture of acid–peptic origin. *Surg. Gynecol. Obstet.* **88**, 560–570.

WEAVER A. W., LARGE A. M. and WALT A. J. (1970) Surgical management of severe reflux oesophagitis. Eight to seventeen year follow-up study. *Am. J. Surg.* **119**, 15–18

Br. J. Surg. Vol. 62 (1975) 608–609

Gastric mucosal resection in the treatment of peptic ulcers: a 1–10 year clinical follow-up

R. M. KIRK*

SUMMARY

The clinical results of gastric mucosal resection are reported after a 1–10-year follow-up in which 76 per cent of patients were followed up for more than 5 years. There were 3 postoperative deaths in 152 patients. Mucosal antrectomy with vagotomy for duodenal ulcer in 96 patients, and for recurrent ulcer in 9 patients, has not been followed by a single recurrence. Gastric mucosal resection alone for the treatment of gastric ulcer in 21 patients resulted in 1 recurrence.

Although vagotomy combined with resection is currently out of fashion for the initial treatment of duodenal ulcer in Britain, mucosal gastric resection has technical advantages in combination with vagotomy for the cure of recurrent ulcers following duodenal ulcer surgery.

MUCOSAL gastric resection is a form of gastrectomy in which the mucosa alone is excised, leaving the other layers of the stomach wall intact. The raw areas are folded away so that mucosal continuity is restored. Mucosal excision is accomplished through a gastroduodenotomy which is then closed after the fashion of a Heineke–Mikulicz pyloroplasty (Kirk, 1965, 1966; Kirk and Sussman, 1972).

Technique

For the treatment of duodenal ulcers mucosal antrectomy is preceded by truncal or selective vagotomy. The extent of mucosal resection for gastric ulcer is equivalent to the formal excision accomplished by Billroth I gastrectomy. When treating recurrent ulcer mucosal antrectomy is combined with truncal vagotomy or the completion of vagotomy.

Gastric mucosal resection is carried out through a gastroduodenotomy. The distal gastric submucosa is infiltrated with an adrenaline in saline solution. The mucosa of the distal stomach is excised, and bleeding points are sealed with diathermy. The posterior gastric and duodenal mucosal edges are then stitched edge to edge, folding the denuded portion of stomach wall backwards. The anterior walls are closed in the manner of a Heineke–Mikulicz pyloroplasty. The raw surfaces are thus excluded so that gastroduodenal mucosal continuity is re-established.

Follow-up

Contact was maintained by requesting patients to post a card annually stating their condition. Symptomatic patients were sent an outpatients' clinic appointment. A comprehensive questionnaire was sent out at 3-yearly intervals. All the patients were assessed independently once or more frequently at least a year after operation. Because the operations were carried out at five widely separated hospitals it was not possible to use a single assessor. For the same reason the final interview was conducted by the author.

Seventeen patients were submitted to acid secretion studies after periods of more than a year after operation. Further operations were performed on 3 patients.

Clinical results were graded by the modified Visick scale described by Goligher et al. (1968). Grade 1 patients were completely asymptomatic. Grade 2 patients had good results but with minor symptoms, easily controlled by dietary adjustments. Grade 3 patients had mild or moderate symptoms not controlled by simple measures. Grade 4 patients had unsatisfactory results because of moderate or severe symptoms or complications which interfered with enjoyment of life or capacity to work. All the patients requiring further surgical procedures were included in this category.

Results

There were 3 (2 per cent) postoperative deaths in 152 patients, from cardiac or respiratory complications. Postoperative bleeding and suture line leaks were not encountered. Subsequent deaths were unrelated to the operation except for a single patient who developed gastric carcinoma after 6 years.

The interval between operation and final interview is set out in *Table I*, together with the number of patients lost from the series. Of 129 patients followed up, 98 (76 per cent) had been operated upon more than 5 years before, and all the primary operations for duodenal ulcers had been carried out at least 3 years before assessment.

There were no recurrences following vagotomy and mucosal antrectomy for the treatment of duodenal ulcers. Also, the combination was effective in the treatment of recurrent ulcers following duodenal ulcer surgery. One patient had recurrence of a gastric ulcer following gastric mucosal resection alone.

The grading of the clinical results is set out in *Table II*. Following vagotomy and mucosal antrectomy for duodenal ulcer in 96 patients, 81 (84·4 per cent) were placed in categories 1 or 2. It was noted during the serial assessment that patients seemed to reach a stable state within 1 year in terms of postoperative symptoms; those with severe symptoms either improved slowly or became more tolerant of

---

* Royal Free Hospital and Willesden General Hospital, London.

Table I: LENGTH OF FOLLOW-UP

Years since operation	No. of operations	Early postoperative deaths	Late deaths	Patients lost	Patients followed up
Up to 10	38	1	5	3	29
9	26	1	3	1	21
8	22		2		20
7	17			2	15
6	15	1		1	13
5	21			1	20
4	7		1		6
3	5			1	4
1–2	1				1
Total	152	3	11	9	129

Patients operated upon up to 3 years before assessment were all suffering from recurrent ulcers following duodenal ulcer surgery or from gastric ulcers. All primary operations for duodenal ulcers were carried out more than 3 years before assessment.

Table II: RESULTS OF 1–10-YEAR FOLLOW-UP

Procedure in addition to mucosal antrectomy	Indication	Visick grade 1	2	3	4	Total
With truncal vagotomy	DU	31	17	8	1	57
With selective vagotomy	DU	23	10	5	1	39
Alone	GU	16	3	1	1	21
With truncal vagotomy	RU	5	3	1		9
As conversion procedure	DU*			3		3
Total	75	75	33	18	3	129

DU, Duodenal ulcer. GU, Gastric ulcer. RU, Recurrent ulcer
* Conversion followed primary duodenal ulcer operation.

them. None of the patients changed substantially after 2 years, even when they were followed up for 10 years.

One patient had such severe postprandial colic and dumping following truncal vagotomy and mucosal antrectomy that he was re-explored, but no cause was found. A patient with quiescent terminal ileitis developed incapacitating diarrhoea following selective vagotomy and mucosal antrectomy, although there was no evidence of recrudescent Crohn's disease. Three patients complained of episodic diarrhoea following truncal vagotomy. Moderate dumping symptoms followed 14 primary and 4 revision operations.

Of 17 patients submitted to insulin tests of gastric secretion at least 1 year after vagotomy and mucosal antrectomy, 16 had negative tests and 1 showed a late positive result.

Discussion

Vagotomy combined with mucosal antrectomy has been an effective combination for the initial treatment of duodenal ulcer, since there was not a single recurrence in 96 patients. It appears to be as effective as vagotomy combined with formal antrectomy in guarding against recurrence, and it results in a low incidence of positive insulin tests (Jordan and Condon, 1970). The Visick grading results are similar to those reported by Goligher et al. (1968) for vagotomy and formal antrectomy, with 84·4 per cent of the patients in the present series falling into categories 1 and 2.

However, Johnston (1974) reported not a single recurrence following 350 operations of highly selective vagotomy (proximal gastric vagotomy) carried out in Leeds and Copenhagen for duodenal ulcers. Kirk (1975) has had 2 recurrences out of 57 patients. Johnston (1975) has emphasized the very low mortality associated with highly selective vagotomy. Unless the long term results of proximal gastric vagotomy without drainage are disappointing, it is likely to become even more popular for the initial surgical treatment of duodenal ulcer.

In the treatment of recurrent ulcer, vagotomy, or completion of vagotomy, combined with mucosal antrectomy, has been effective in curing 9 patients. It has a technical advantage in patients who have previously been submitted to gastric surgery that the mucosal resection can be performed entirely from within the stomach without the need to ligate and divide a single major blood vessel.

References

GOLIGHER J. C., PULVERTAFT C. N., DE DOMBAL F. T., CONYERS J. H., DUTHIE H. L., FEATHER D. B., LATCHMORE A. J. C., SHOESMITH J. H., SMIDDY F. G and WILLSON-PEPPER J. (1968) Five- to eight-year results of Leeds/York controlled trial of elective surgery for duodenal ulcer. *Br. Med. J.* **1**, 781–787.

JOHNSTON D. (1974) Highly selective vagotomy. *Gut* **15**, 748–757.

JOHNSTON D. (1975) Operative mortality and postoperative morbidity of highly selective vagotomy. *Br. J. Surg.* **62**, 160.

JORDAN P. H. jun. and CONDON R. E. (1970) A prospective evaluation of vagotomy-pyloroplasty and vagotomy-antrectomy for the treatment of duodenal ulcer. *Ann. Surg.* **172**, 547–563.

KIRK R. M. (1965) Mucosal antrectomy with vagotomy in the treatment of duodenal ulcer. *Br. J. Surg.* **52**, 604–606.

KIRK R. M. (1966) Mucosal antrectomy in the treatment of peptic ulcer. *Proc. R. Soc. Med.* **59**, 571–575.

KIRK R. M. (1975) Truncal, selective, and proximal gastric vagotomy without drainage, related to the size of the pyloroduodenal canal. *Proc. R. Soc. Med.* **68**, 179–180.

KIRK R. M. and SUSSMAN T. (1972) Vagotomy and mucosal antrectomy in the elective treatment of duodenal ulcers. *Am. J. Surg.* **123**, 323–328.

Br. J. Surg. Vol. 62 (1975) 610–617

Abdominal tuberculosis: demonstration of tubercle bacilli in tissues and experimental production of hyperplastic enteric lesions

PRITAM DAS AND H. S. SHUKLA*

SUMMARY

Material obtained from 35 cases of abdominal tuberculosis was studied and an attempt was made to demonstrate tubercle bacilli by special staining of histological sections, culture and guinea-pig inoculation.

Acid fast bacilli could be demonstrated in 80 per cent of cases. The remaining cases were also possibly due to tuberculous infection because granulomas with Langhans's type of giant cells and caseation or calcification of lymph nodes were present. The bacilli were demonstrated in bowel tissue showing non-specific histology in 1 case. In 2 other cases with non-specific lesions in the bowel the bacilli were demonstrated in lymph nodes.

Guinea-pig inoculation studies showed that hypertrophic lesions of the bowel with a non-specific type of reaction could develop after intraperitoneal injection of tubercular material.

Although it cannot be said on the basis of this study that Crohn's disease is caused by tuberculous infection, it can be concluded that tuberculous infection can give rise to a Crohn's type of lesion.

SINCE Crohn et al. (1932) described regional ileitis a controversy has arisen and many have doubted even the existence of hyperplastic enteric tuberculosis. Warren and Sommers (1948), Manglik and Misra (1952) and Gupta et al. (1962) came to the conclusion that the so-called ileocaecal tuberculosis was a non-specific granulomatous lesion. They were unable to demonstrate tubercle bacilli in any of their specimens. Taylor (1945), Anand (1956), Bruce (1959), Paustian and Bockus (1959) and Chandra and Basu (1967) presented the opposite view and doubted if regional ileitis was a separate pathological process. Taylor (1945) considered hyperplastic ileocaecal tuberculosis and regional ileitis to be different responses of the host to infection with tubercle bacilli, and Anand (1956) opined that bowel changes in regional ileitis may well be due to modification of tubercular enteritis by anti-tubercular drugs, increased host resistance and low virulence of organisms. Florey (1954) observed that productive tubercular lesions without caseation may occur in patients with low sensitivity and high immunity to tubercle bacilli. Reiks and Washington (1962) and Prakash et al. (1970) observed that an atypical strain of mycobacteria may produce a variable morphological picture in the intestine. The differentiation between these two conditions on clinical grounds, and even on histological examination of resected tissues, is difficult, as reported by many workers (Anderson and Munro, 1932; Crohn and Yarnis, 1940; Tribedi and Gupta, 1941; Ukil, 1942; Warren and Sommers, 1948; Taylor, 1945; Hoon et al., 1950; Anand, 1956; Brenner et al., 1970; Tandon and Prakash, 1972). Therefore, the demonstration of tubercle bacilli in the tissues assumes utmost importance in the diagnosis of these lesions.

In the present study an attempt was made to identify the tubercle bacilli in the tissues on histological examination, by culture of the tissues and by guinea-pig inoculation. Typing and drug sensitivity of the bacilli were also done. During this investigation hyperplastic intestinal lesions were discovered in guinea-pigs.

Materials and methods

Material removed from 35 patients with abdominal tuberculosis admitted to SRN Hospital, Allanhabad, India, during 1973 was studied. Immediately after removal of the tissue, specimens for culture and guinea-pig inoculation were deep frozen, while the rest was placed in 10 per cent formol saline. The following examinations were subsequently carried out:

1. *Histological examination* of resected tissues or biopsy specimen was done in 66 cases: mesenteric nodes 18, bowel 10, peritoneum 21, omentum 3, cold abscess wall 1, liver biopsy 8 and endometrium 5. Paraffin sections were prepared using xyline as clearing agent. The sections were stained with haematoxylin and eosin.
2. *Demonstration of acid fast bacilli in tissue sections*: Fifty-one specimens were stained by the modified Ziehl–Neelsen method (Cruickshank, 1970) for demonstration of tubercle bacilli.
3. *Culture of acid fast bacilli*: Petroff's modified method (Cruickshank, 1970) was employed for concentrating tubercle bacilli in tissues. Inoculation was done on Lowenstein–Jensen medium. Cultures were made from 31 samples: mesenteric lymph nodes 11, bowel 7, ascitic fluid 8, wound discharge 1, peritoneum 2, omentum 2.
4. *Guinea-pig inoculation* was performed with tissue concentrate prepared for culture as above from 19 samples: mesenteric nodes 4, bowel 8, peritoneal fluid 4, peritoneum 3. The concentrate was injected intraperitoneally and each animal was kept strictly isolated

---

*Department of Surgery, MLN Medical College, Allahabad, India.

for 6 weeks, when they were sacrificed. Five animals died within 2 weeks. Autopsy was done in all the animals and viscera were examined for tubercular lesions by naked eye and microscopic examination. Tissue sections were stained for tubercle bacilli.

5. *Drug sensitivity* was tested in 14 cases by the method of Cruickshank (1970) against streptomycin, isonicotinic acid hydrazide, para-aminosalicyclic acid, ethambutal, cycloserine and thiosemicarbazone.

6. *Type verification of Mycobacterium tuberculosis* into human, bovine and anonymous varieties was done in 14 cases by the method of Marks (1964) and Cruickshank (1970) on the basis of growth on Lowenstein–Jensen medium, catalase activity, drug sensitivity and reaction in guinea-pigs. Growth of the organisms was observed in normal light at room temperature, 37 °C and 43 °C, and in complete darkness at 37 °C.

Observations

The various lesions observed clinically or at laparotomy were stricture of the ileum 8, hyperplastic caecal lesions 3, stricture of the colon 2, mesenteric lymphadenitis 2, chronic tuberculous peritonitis 14 and tuberculous ascites 6, giving a total of 35 lesions. The grouping was done according to the dominant lesion observed clinically or at the time of operation.

Bowel lesions

Of the 13 cases in which bowel was involved, a resected bowel specimen along with mesentery was available in 10, lymph nodes only in 2 and a piece of peritoneum alone in 1 case. Naked eye examination showed a few unusual features worthy of note.

1. Mesenteric fat was increased in all cases; in some the fat extended on to the bowel, a feature which has been described as typical of regional ileitis (Valdes-Dapena, 1966).

2. In 2 cases the mucosal ulcer crater had become epithelialized.

3. In 1 case a pseudopolyp was present at the site of the stricture.

4. Small superficial ulcers were present on the mucosa proximal to the site of lesion in 4 cases (*Fig.* 1). These lesions have also been described as typical of regional ileitis (Valdes-Dapena, 1966).

Histological examination of the bowel showed a tubercular granuloma with caseation in 2 cases, granuloma with giant cells but no caseation in 4 and a non-specific type of granuloma without caseation and without giant cells in 4 cases (*Table I*). Some of the unusual features on histological examination of the bowel were:

1. The three types of granuloma could be seen on the same slide at different places (*Fig.* 2), indicating that any one of the three types of histological picture could be produced by tubercular infection of the bowel.

2. Granulomas were found in the submucous as well as in the muscle layer.

3. Diffuse infiltration of chronic inflammatory cells as opposed to localized granulomas was also present in all the bowel layers in positively tubercular lesions.

4. Granulation tissue could be seen extending from the mucosa to the serosa in some of the slides (*Fig.* 3).

5. All the 4 cases showing a non-specific type of lesion had had anti-tubercular treatment prior to operation.

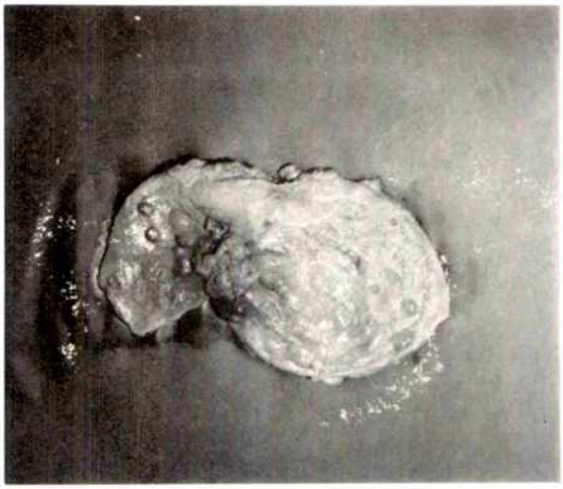
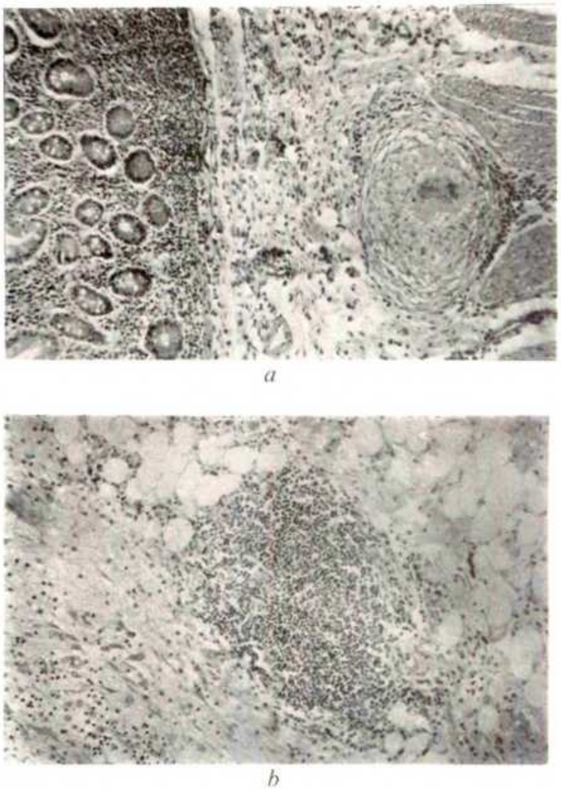


Fig. 1. Photograph of mucosal surface of resected bowel showing small superficial ulcers proximal to the main lesion.



a

b

Fig. 2. Photomicrographs of a section of bowel showing (*a*) tubercular granuloma with giant cells, and (*b*) non-specific type of inflammatory reaction. Both types of lesions were present in the same section.

Table I: HISTOLOGICAL AND BACTERIOLOGICAL FEATURES OF BOWEL LESIONS

Case no.	Specimen	Microscopic examination			AFB in tissues	AFB on culture	AFB on guinea-pig inoculation	Previous anti-tubercular treatment
		Bowel	Lymph node	Peritoneum				
15	Stricture of ileum	Granuloma with giant cells	Caseation present		Bowel+ Lymph node−	Bowel− Lymph node−	Bowel+	No
16	Stricture of ileum	Granuloma with caseation	Caseation present	Caseation present	Bowel+ Lymph node+ Peritoneum+	Bowel+ Lymph node−	Not done	No
17	Stricture of ileum		Granuloma with giant cells		Lymph node−	Not done	Not done	No
19	Stricture of ileum	Non-specific granuloma	Calcified		Bowel− Lymph node−	Bowel− Lymph node−	Bowel−	Yes
20	Stricture of ileum		Caseation present	Non-specific granuloma	Lymph node+	Not done	Not done	Yes
31	Stricture of ileum	Granuloma with giant cells. No caseation			Bowel−	Bowel+	Animal died early	No
34	Stricture of ileum	Non-specific granuloma	Caseation present		Lymph node+ Bowel−	Bowel−	Bowel−	Yes
37	Stricture of ileum			Granuloma with giant cells	Peritoneum−	Peritoneal fluid+	Not done	No
24	Hypertrophic caecum	Non-specific granuloma	Granuloma with giant cells		Bowel+ Lymph node+	Bowel− Lymph node+	Bowel−	Yes
29	Hypertrophic caecum	Non-specific granuloma	Granuloma with giant cells		Bowel− Lymph node−		Bowel−	Yes
33	Hypertrophic caecum	Granuloma with caseation	Granuloma with giant cells		Bowel+ Lymph node−	Lymph node+	Lymph node+	No
2	Stricture of colon	Non-specific granuloma	Caseation present	Normal	Bowel− Lymph node+	Bowel−	Died early	Yes
25	Stricture of colon	Granuloma with giant cells	Caseation present		Bowel− Lymph node+			No

AFB, Acid fast bacilli: +, bacilli present; −, bacilli absent.

Tubercle bacilli were demonstrated in the bowel in 3 cases on histological examination, culture of tissue or guinea-pig inoculation (*Table I*). In the other 5 bowel specimens the tubercle bacilli could not be demonstrated in the bowel wall but they were demonstrated in the lymph nodes in 2 and in the peritoneal fluid in 1. Thus, there were 2 cases in which tubercle bacilli were not demonstrated in any of the tissues examined. In one the lymph node examined was calcified, and in the other a granuloma with giant cells was present in the lymph node. Both these cases had a non-specific lesion in the bowel.

Of the 3 cases of bowel involvement in which a resected bowel specimen was not available, one showed tubercle bacilli in a lymph node, one had tubercle bacilli in the peritoneal fluid and in one there was a giant cell granuloma in a lymph node but no tubercle bacilli could be demonstrated.

Mesenteric lymphadenitis

Tuberculous mesenteric lymphadenitis without any obvious bowel lesion was present in 2 cases (*Table II*); both of them presented as cold abscesses in the mesentery. Histological examination showed a tubercular granuloma with caseation in one case, and a granuloma with giant cells but no caseation in the other. Acid fast bacilli were demonstrated in the tissues in both cases. Neither had had anti-tubercular treatment before operation.

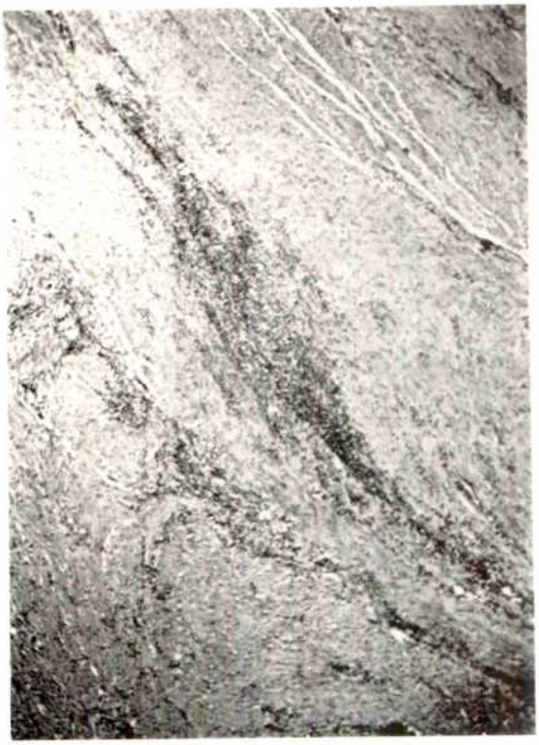


Fig. 3. Photomicrograph of a bowel lesion showing extension of granulation tissue from mucosa to serosa.

Table II: FINDINGS IN MESENTERIC LYMPHADENITIS

Case no.	Histology	AFB in tissues	AFB on culture	AFB on guinea-pig inoculation	Previous anti-tubercular treatment
11	Lymph node, granuloma with giant cells Peritoneum, non-specific granuloma	Lymph node + Peritoneum +	Lymph node +	Lymph node +	No
22	Lymph node, caseous	Lymph node +	Not done	Not done	No

Table III: FINDINGS IN CHRONIC MILIARY TUBERCULOUS PERITONITIS

Case no.	Histology	AFB in tissues	AFB on culture	AFB on guinea-pig inoculation	Previous anti-tubercular treatment
1	Peritoneum, caseous	Peritoneum +			No
4	Lymph node, caseous	Lymph node +	Lymph node −		No
5	Lymph node, caseous Peritoneum, granuloma with giant cells Liver, fatty change	Lymph node + Peritoneum +	Lymph node +		No
6	Peritoneum, non-specific granuloma Omentum, non-specific Liver, fatty change	Omentum + Peritoneum −			No
7	Peritoneum, non-specific granuloma Liver, normal	Peritoneum +	Omentum +	Peritoneum +	No
9	Peritoneum, caseous Liver, caseous Lymph node, caseous	Peritoneum + Lymph node +	Lymph node +	Lymph node +	No
12		Wound discharge +		Died early	No
14	Lymph node, caseous Peritoneum, granuloma with giant cells	Lymph node + Peritoneum +	Fluid culture		No
23	Peritoneum, granuloma with giant cells	Peritoneum +	Peritoneum + Omentum +	Died early	Yes
26	Peritoneum, non-specific granuloma Lymph node, non-specific granuloma	Peritoneum + Lymph node +			No
30	Peritoneum, granuloma with giant cells	Peritoneum +			No
32	Peritoneum, granuloma with caseation	Peritoneum −	Peritoneum −	Not done	Yes
35	Peritoneum, granuloma with giant cells	Peritoneum −	Peritoneum −	Peritoneum +	No
36	Omentum, granuloma with giant cells	Omentum −	Not done	Not done	No

Table IV: FINDINGS IN ASCITIC CASES

Case no.	Histology	AFB in tissues	AFB in fluid smear	AFB in fluid culture	AFB on guinea-pig inoculation	Previous anti-tubercular treatment
2	Peritoneum, granuloma with giant cells Liver, fatty change	Peritoneum —	+	—	Died early	No
8	Peritoneum, caseous Lymph node, caseous	Lymph node + Peritoneum —	— —	Lymph node +	Lymph node +	Yes
13	Not done	Not done	—	+*	Not done	No
21	Peritoneum, giant cells in granuloma	Peritoneum —	—	—	Fluid +	No
27	Peritoneum, granuloma with giant cells	Peritoneum —	—	—	Not done	No
38	Peritoneum, granuloma with giant cells	Peritoneum —	—	—	Not done	Yes

* Anonymous AFB.

Table V: POSITIVE CULTURES IN TISSUES AND FLUIDS

Tissue or fluid cultured	Total no.	No. in which AFB grown	%
Mesenteric lymph nodes	11	6	54·5
Bowel	7	2	42·8
Ascitic fluid and wound discharge	9	4	44·4
Peritoneum/omentum	4	2	50·0
Total	31	15	48·4

Chronic miliary tuberculous peritonitis

There were 14 cases in which the dominant feature on opening the abdomen was the presence of widespread multiple tubercles on the peritoneal surface. There was no apparent lesion of the bowel. Lymph node enlargement was also not a dominant feature. A piece of peritoneum was available in 11 cases, lymph nodes in 4, needle biopsy of the liver in 4, a piece of omentum in 3 and peritoneal fluid in 1. In the 3 cases in which a piece of peritoneum was not available, wound discharge was available in 1, a lymph node in 1 and omentum in the third case.

Histological examination of the peritoneal pieces showed caseation in 3 cases, a granuloma with giant cells in 5 and a non-specific granuloma in 3 cases. Liver biopsy showed caseation in 1, fatty change in 2 and normal parenchyma in 1 (*Table III*). The omentum showed granuloma with giant cells.

In the 14 cases of chronic miliary tuberculous peritonitis, tubercle bacilli were demonstrated in 12 cases (*Table III*), including 3 cases in which the histological picture was of non-specific inflammation. The wound discharge and the peritoneal fluid were positive for acid fast bacilli. In the remaining 2 cases acid fast bacilli were not demonstrated in any specimen; one had a granuloma with caseation in the peritoneum and the other showed a granuloma with giant cells on omental biopsy. Unfortunately guinea-pig inoculation was not done in one of these cases and guinea-pig inoculation and culture were not done in the other case.

Ascites

In this group 6 cases with fluid distension of the abdomen were included. Biopsy samples of peritoneum were available in 5 cases along with ascitic fluid in 5, needle biopsy of the liver in 2 and a lymph node in 1 case. Ascitic fluid was available in the case for which there was no peritoneal biopsy.

Histology of the peritoneal biopsy showed caseation necrosis in 1 and granuloma with giant cells in 4 cases. The lymph node showed caseation. This was the same case in which the peritoneum had shown caseation (*Table IV*).

Tubercle bacilli were demonstrated in a lymph node in 1 case and in the ascitic fluid in 3 cases. The 2 cases in which tubercle bacilli were not demonstrated had granulomas with giant cells on histological examination (*Table IV*).

Culture results

Of the 31 specimens cultured, 15 (48·4 per cent) yielded positive results (*Table V*). The bowel yielded the least percentage of positive cultures (2 out of 7), while the mesenteric nodes and peritoneal fluid yielded positive results in 6 out of 11 and 4 out of 9 cases respectively. It has to be emphasized that 4 of the 7 bowel cases had had anti-tubercular treatment, and 2 of the 3 cases who had had no anti-tubercular treatment yielded a positive bowel culture.

Typing of the acid fast bacilli

Thirteen of the 14 cultures tested were found to be of the human variety. In 1 case the bacilli grown from ascitic fluid were the anonymous type.

Drug sensitivity

Drug sensitivity was tested in 14 cultures (*Table VI*). The bacilli were resistant to streptomycin in 8, to para-aminosalicyclic acid in 8, to ethambutal in 4, to isonicotinic acid hydrazide and cycloserine in 1 each and to thiosemicarbazone in none. Surprisingly, 11 of these patients had had no anti-tubercular treatment, and in the 1 patient who had received anti-tubercular treatment the bacilli were sensitive to all these anti-tubercular drugs except para-aminosalicylic acid, which she had not been given.

Guinea-pig inoculation

Nineteen guinea-pigs were inoculated with tissue extract. Five of these died within 1–2 weeks, before the tubercular lesion had had time to develop. Of the remaining 14 animals, 10 developed tubercular lesions and 4 did not. Nine cases which showed a positive guinea-pig test were also positive on tissue culture or acid fast staining of tissue sections. One case was positive on guinea-pig inoculation alone so that guinea-pig inoculation did add to the diagnostic accuracy to a small extent. There were 2 cases in which the guinea-pig inoculation of the bowel was negative while the histological section showed tubercle bacilli.

The various lesions found in the guinea-pigs are shown in *Table VII*. It can be observed that none of the animals developed a lesion in the peritoneum, 8 showed caseous mesenteric nodes, 4 had caseous tubercles in the liver and 8 had caseous tubercles in the spleen. An interesting feature was the development of hyperplastic intestinal lesions in the bowel in 4 animals. The segment of the terminal ileum involved was 3–5 mm in length. The bowel was visibly and palpably thickened and histological examination showed a non-specific lesion. Two showed tubercle bacilli in these lesions on acid fast staining, and the mesenteric nodes were positive for acid fast bacilli. The significance of this observation is considerable in that the hypertrophic bowel lesion could occur from infection from the peritoneum, and these lesions may or may not show the organisms. The tubercle bacilli were seen in large numbers in tissues of guinea-pigs and the bacilli were comparatively longer.

Discussion

Bowel lesions

There were 4 specimens of bowel in which the microscopic picture was of the non-specific type. These patients had had anti-tuberculous treatment for periods ranging from 27 days to 2 years. In 2 cases tubercle bacilli were seen on the histological section of

Table VI: TYPE OF BACILLI AND THEIR DRUG SENSITIVITY

Case no.	Type	Streptomycin	PAS	INH	Ethambutal	Cycloserine	Thiosemi-carbazone
5	Human	R	R	S	R	R	S
7	Human	S	S	S	S	S	S
8	Human	S	R	S	S	S	S
9	Human	R	S	S	S	S	S
11	Human	R	R	S	R	S	S
12	Human	R	R	S	R	S	S
13	Anonymous	R	R	R	R	S	S
14	Human	R	S	S	S	S	S
16	Human	S	R	S	S	S	S
24	Human	S	S	S	S	S	S
31	Human	S	S	S	S	S	S
32	Human	R	R	S	S	S	S
33	Human	S	R	S	S	S	S
37	Human	R	S	S	S	S	S

PAS, Para-aminosalicylic acid. INH, Isonicotinic acid hydrazide. R, Resistant. S, Sensitive.

Table VII: LESIONS OCCURRING IN THE GUINEA-PIGS

Case no.	Mesenteric lymph nodes	Liver	Spleen	Bowel	Lungs	Kidney	Peritoneum
7	Caseous. AFB present	No lesion	Caseous tubercles	No lesion	No lesion	No lesion	No lesion
8	Caseous. AFB present	Caseous tubercles	Hypertrophy of lymphoid follicles	Hypertrophic lesion. No caseation. No giant cells. AFB present	No lesion	No lesion	No lesion
9	Caseous. AFB present	Caseous tubercles	Caseous tubercles. AFB present	Non-specific hypertrophic lesion. No AFB	No lesion	No lesion	No lesion
10	Caseous. AFB present	Caseous tubercles	Caseous tubercles. AFB present	Non-specific hypertrophic lesion. No AFB	No lesion	No lesion	No lesion
21	Lymphoid follicular hyperplasia. No AFB	No lesion	Caseous tubercles. AFB present	No lesion	No lesion	No lesion	No lesion
14	Caseous. AFB present	No lesion	Caseous tubercles	No lesion	No lesion	No lesion	No lesion
15	Caseous. AFB present	No lesion	No lesion	No lesion	No lesion	No lesion	No lesion
16	Caseous. AFB present	Caseous tubercles	Caseous tubercles	Non-specific hypertrophy. AFB present	Caseous tubercles	No lesion	No lesion
19	No lesion	No lesion	No lesion	No lesion	No lesion	No lesion	No lesion
24	No lesion	No lesion	No lesion	No lesion	No lesion	No lesion	No lesion
29	No lesion	No lesion	No lesion	No lesion	No lesion	No lesion	No lesion
33	Non-specific. AFB not seen	Normal	Caseous. AFB seen	No lesion	No lesion	No lesion	No lesion
34	Non-specific. No AFB	Normal	No lesion	No lesion	No lesion	No lesion	No lesion
35	Caseous. AFB seen	Normal	Caseous. AFB seen	No lesion	No lesion	No lesion	No lesion

Table VIII: PRESENCE OF AFB ACCORDING TO HISTOLOGICAL FINDINGS

Histological findings	Total no. of tissues	No. in which AFB seen	%
Non-specific granuloma	11	5	45·4
Granuloma with giant cells. No caseation necrosis	20	8	40
Granuloma with caseation necrosis	20	16	80
Total	51	29	56·8

a regional lymph node. In the other 2 no tubercle bacilli were demonstrated by histological section, tissue culture or guinea-pig inoculation. These cases could be regarded as regional enteritis. We are inclined to believe them to be tuberculous because in one a regional lymph node showed a granuloma with giant cells, and in the other the lymph node was calcified. Several workers have reported that anti-tubercular therapy alters the histology to a non-caseous granuloma (Taylor, 1945; Wig and Bawa, 1953; Anand, 1956). In addition to these observations, we have to add that a caseating granuloma and a non-specific type of granuloma may be present on the same histological slide of bowel. Confluent granulomas and transmural infiltration of bowel wall, which are more frequent in tuberculosis than in Crohn's disease (Howell and Knanpton, 1964; Hawley et al., 1968), were also observed in our cases. We cannot say that Crohn's disease is caused by infection of tubercle bacilli, but tuberculous infection can cause an inflammatory reaction similar to that of Crohn's disease.

Demonstration of acid fast bacilli

We have been able to demonstrate tubercle bacilli on histological slides in 80 per cent of tissues showing caseation, in 40 per cent of tissues showing granuloma with giant cells and in 45·4 per cent of tissues showing non-specific granuloma (*Table VIII*). The tubercle bacilli in the tissues showed variable morphology. Some of them were long and beaded, some were short and straight and others were long and curved. In caseous areas the bacilli were seen in and around the area of caseation. The bacilli were sparsely distributed and required prolonged search. Anand (1956), Hancock (1958), Howel and Knanpton (1964) and Lee and Roy (1964) showed that there is no correlation between caseation and positive culture growth. This was not so in our cases. Wig and Bawa (1953) obtained growth of tubercle bacilli in 26 out of 88 cases, and Prakash et al. (1974) obtained growth in 11 out of 95 cases. In our study we were able to obtain a positive culture in 15 out of 31 specimens, probably the highest figure obtained so far by any worker. Six out of 11 mesenteric nodes and 2 out of 7 bowel specimens showed a positive culture growth in our cases.

Considering all the examinations done, we were able to demonstrate tubercle bacilli in 28 (80 per cent) out of 35 cases studied. A more thorough search could have resulted in a higher incidence of positive results. Culture or guinea-pig inoculation was not done in all cases, and these procedures might have yielded tubercle bacilli.

Experimental production of hyperplastic lesions

Attempts have been made to produce abdominal tuberculosis in guinea-pigs. Oral feeding with infected material results in the production of ulcerative intestinal lesions. Klebs (1868) and Anguli and Menon (1950) produced bowel lesions by feeding guinea-pigs with infected material. They also removed the regional lymph nodes and came to the conclusion that lymphatic obstruction resulted in non-specific ulceration of the bowel segment concerned and an increase in subserous fat. The intraperitoneal injection of tubercular material results in infection of the liver, spleen, lymph glands and lungs. We have not come across any report describing bowel lesions after intraperitoneal injection. It was therefore of considerable interest when hypertrophic intestinal lesions were detected in the present study in 4 of the animals. Histological examination of these lesions showed a non-specific type of response. Acid fast staining of the sections yielded tubercle bacilli in 2. In the other 2 animals acid fast bacilli were detected in the regional lymph nodes. It is evident from these findings that tubercle bacilli can cause a hypertrophic lesion of the bowel with a non-specific type of inflammatory reaction. Further, the organism may or may not be detected, and the infection may not come from the lumen of the bowel. This observation also lends support to the idea that the caecal lesion may be produced by infection from the Fallopian tubes.

The type and resistance of the organisms

Contrary to the belief that bovine infection should be more frequent in bowel lesions, it was found that all the organisms detected in the bowel in this study were of the human type. Only 1 case had mycobacteria of anonymous type, which is reputed to be rarely pathological. It was found in the ascitic fluid.

The organisms were resistant to the various anti-tubercular drugs even in patients who had never had treatment with any of these drugs. Obviously they were resistant from the very beginning. Apparently isonicotinic acid hydrazide gives rise to minimal resistant types, because only 1 case had organisms resistant to this drug, in spite of the fact that it has been in use for more than two decades.

Acknowledgements

We are grateful to Dr T. N. Mehrotra, Professor of Pathology, Dr S. C. Gupta, Reader in Pathology, and Dr R. C. Pandey, Lecturer in Microbiology, of MLN Medical College, Allahabad, for continual help and guidance in this study.

References

ANDERSON J. and MUNRO W. T. (1932) Tuberculous hyperplasia of the large intestines (human tubercle bacillus). A report of a case with unusual features. *Br. J. Surg.* **20,** 331–336.

ANGULI V. C. and MENON C. P. V. (1950) Ileo-colic tuberculosis and non-specific ulceration. *Ind. J. Surg.* **12**, 208.

ANAND S. S. (1956) Hypertrophic ileocaecal tuberculosis in India with a record of 50 hemicolectomies. *Ann. R. Coll. Surg. Engl.* **19**, 205–222.

BANERJI B. N. (1950) Chronic hyperplastic ileocaecal tuberculosis. *Ind. J. Surg.* **12**, 33.

BRENNER S. M. ANNES G. and PARKER J. G. jun. (1970) Tuberculous colitis simulating non-specific granulomatous disease of the colon. *Am. J. Dig. Dis.* **15**, 85–92.

BRUCE J. (1959) Surgical commentary on the disorders of small intestines. *Proc. R. Soc. Med.* **52**, 42–46.

CHANDRA A. and BASU A. K. (1967) Cicatrising lesion of ileocaecal tuberculosis. *Ind. J. Surg.* **29**, 645–659.

CROHN B. B., GINGBURG L. and OPPENHEIMER G. D. (1932) Regional ileitis, a pathologic and clinical study. *JAMA* **99**, 1323–1329.

CROHN B. B. and YARNIS H. (1940) Primary ileocaecal tuberculosis. *N Y J. Med.* **40**, 158.

CRUICKSHANK R. (1970) *Medical Microbiology*. Edinburgh, Livingstone, pp. 202, 653–656.

FLOREY H. (1954) *Lectures on General Pathology*. Lloyd-Luke, London.

GUPTA R. S., CHATTERJEE A. K., ROY R. and GHOSH B. N. (1962) A review of the result of treatment of 44 cases of Crohn's disease. *Ind. J. Surg.* **24**, 797–805.

HANCOCK D. M. (1958) Hyperplastic tuberculosis of the distal colon. *Br. J. Surg.* **46**, 63–68.

HAWLEY P. R., WOOLFE H. R. and FULLERTON J. M. (1968) Hypertrophic tuberculosis of the rectum. *Gut* **9**, 461–465.

HOON J. R., DOCKERTY M. B. and PEMBERTON J. (1950) Ileocaecal tuberculosis including a comparison of this disease with non-specific regional enterocolitis and non-caseous tuberculated enterocolitis. *Int. Abstr. Surg.* **91**, 417–440.

HOWELL J. S. and KNANPTON P. J. (1964) Ileocaecal tuberculosis. *Gut* **5**, 524–529.

KLEBS A. C. (1868) quoted by BOCKUS H. L. (1966) *Gastroenterology*, Vol. V. Philadelphia, Saunders, p. 312.

LEE F. D. and ROY A. D. (1964) Ileocaecal granuloma. *Gut* **5**, 517–523.

MARKS J. (1964) The anonymous mycobacteria. In: DYKES S. C. *Recent Advances in Clinical Pathology IV*. London, Churchill, pp. 2–12.

MANGLIK V. S. and MISRA S. C. (1952) Primary intestinal tuberculosis. *J. Ind. Med. Assoc.* **22**, 12.

PAUSTIAN F. F. and BOCKUS H. L. (1959) So called "primary ulcerohypertrophic ileocaecal tuberculosis". *Am. J. Med.* **27**, 509–518.

PRAKASH A., TANDON H. D., NIRMALA L., WADWA S. N., PRAKASH OM and KAPOOR M. (1970) Chronic ulcerative lesions of bowel. *Ind. J. Surg.* **30**, 1.

REIKS H. and WASHINGTON W. (1962) Comparative pathology of lesions produced by atypical mycobacterium. *Am. J. Clin. Pathol.* **38**, 244–250.

SHARMA G. C., KALA P. C. and BHARGAWA U. (1972) Obstructive tuberculous lesions of the large gut. *Am. J. Proctol.* **23**, 218.

TANDON H. D. and PRAKASH A. (1972) Pathology of intestinal tuberculosis and its distinction from Crohn's disease. *Gut* **13**, 260–269.

TAYLOR A. W. (1945) Chronic hyperplastic ileocaecal tuberculosis, and its relation to regional ileitis (Crohn's disease). *Br. J. Surg.* **33**, 178–181.

TRIBEDI B. P. and GUPTA D. M. (1941) Intestinal tuberculosis in Bengal. *J. Ind. Med. Assoc.* **11**, 41–44.

UKIL A. C. (1942) Early diagnosis and treatment of intestinal tuberculosis. *Ind. Med. Gaz.* **77**, 613.

WARREN S. and SOMMERS S. C. (1948) Cicatrizing enteritis (regional ileitis) as a pathological entity. Analysis of 120 cases. *Am. J. Pathol.* **24**, 475–501.

WIG K. L. and BAWA Y. S. (1953) Abdominal tuberculosis unassociated with acute pulmonary tuberculosis. *Ind. Tuber.* **1**, 6.

VALDES-DAPENA A. (1966) Pathology of regional enteritis. In: BOCKUS H. L. *Gastroenterology*, Vol. II. Philadelphia, Saunders, pp. 232–242.

Br. J. Surg. Vol. 62 (1975) 618–620

Primary gastric tuberculosis: a case report

R. E. PAGE, R. E. WILLIAMS AND E. A. BENSON*

SUMMARY

A case of primary gastric tuberculosis is reported in a 34-year-old Negro male. The difficulty in diagnosis is emphasized. Surgical resection with postoperative anti-tuberculosis chemotherapy was followed by satisfactory recovery.

Case report

A 34-year-old West Indian labourer, resident in the United Kingdom for 13 years, attended his general practitioner complaining of dyspepsia, and was treated with antacids for a year before a small haematemesis resulted in a surgical outpatients' consultation. A barium meal examination failed to demonstrate any abnormality and the patient was given a further supply of antacids. He was followed up in the outpatients' clinic and continued to complain, and 10 months later when reviewed he had obviously lost weight and examination revealed a gastric succussion splash. A repeat barium meal study (*Fig.* 1) now showed a constant filling deformity in the antral region; no ulcer crater could be identified. A chest X-ray was normal. The patient was admitted to hospital, and at gastroscopy a flat sloughing lesion in the pyloric antrum was visualized but its nature was obscure. Laparotomy revealed a firm infiltrating lesion, low on the lesser curve of the stomach in association with marked lymph node enlargement around the coeliac axis and the left gastric artery; similar enlarged nodes were found in the subpyloric region. In the terminal ileum an infiltrating lesion measuring slightly less than 1 cm in width encircled the bowel. An operative diagnosis of carcinoma of the stomach with secondaries in the terminal ileum was made, and what was felt to be palliative surgery took the form of partial gastrectomy (resecting the gastric lesion but leaving many involved glands around the coeliac axis) together with a small bowel resection.

The pathologist submitted the following report: 'Two specimens were received, firstly a funnel of stomach 11 × 11 cm bearing an ulcer 2 cm in diameter. The adjacent lymph nodes were enlarged and contained creamy material. Secondly, a tube of small intestine 35 cm long × 5 cm diameter with a haemorrhagic fusiform swelling 1 cm in diameter encircling and extending through the wall.

'Microscopy of both specimens showed an acute and chronic inflammatory reaction with, in places, collections of epithelioid cells and Langhans's giant cells (*Fig.* 2). In addition, the lymph nodes showed caseous necrosis (*Fig.* 3).

'Staining of the sections by an auramine phenol fluorescent technique (Greenwood and Fox, 1973) showed the presence of tubercle bacilli in the lesion. These were not confirmed using the Ziehl–Neelsen method.

'In view of the histological picture and fluorescent microscopy a diagnosis of tuberculosis was made. Unfortunately, bacteriological confirmation was not possible as only formalin-fixed material was received (Walter and Israel, 1974).'

The patient was started on streptomycin 0·750 g daily and Mynah 250 (ethambutol and isoniazid) 1 tablet t.d.s., and postoperatively made satisfactory progress and was discharged to a convalescent hospital on the twelfth day. A Mantoux test performed postoperatively was positive, but stool examination did not show any acid-fast bacilli. A repeat chest X-ray failed to demonstrate any pulmonary tuberculosis, and three early morning specimens failed to produce any tubercle bacilli.

The patient was well and gaining weight when seen 4 months after his operation.

Discussion

Primary tuberculosis of the stomach is surpassed in rarity only by a primary lesion involving the oesophagus. Isolated cases of tuberculosis limited to the stomach have appeared in the Russian (Kuzionov and Polinkova, 1973) and Indian (Wig et al., 1961) literature, but in the Western world the condition is extremely rare. The only case of primary gastric tuberculosis to be reported in the Western literature has been by Stirk (1968). Palmer (1950), in 20 585 post-mortem examinations performed on patients dying with pulmonary tuberculosis, found the stomach to be involved in only 0·5 per cent, and in a recent series from South Africa (Novis et al., 1973) only 1 of 59 patients with gastro-intestinal tubercle had involvement of the stomach.

Tuberculosis of the stomach is usually secondary to a primary focus involving another organ, invariably the lungs (Palmer, 1950), and tends to be a feature of widespread disease. The case presented in this communication had no pulmonary or pharyngeal involvement.

The incidence of pulmonary disease diagnosed radiologically in patients with established gastro-intestinal tuberculosis varies from series to series. Hamandi and Thamer (1965), in a study of 86 patients with gastro-intestinal tuberculosis, found only 10 with pulmonary involvement, whereas Novis et al. (1973) demonstrated a pulmonary lesion in 20 out of 56 patients. Abrams and Holden (1964) showed that 56 per cent of patients with pulmonary tuberculosis also have involvement of some part of the gastro-intestinal tract.

The factors protecting the stomach against invasion by tubercle bacilli have been listed by Good (1931). It has, however, been suggested by Kossick (1969) that the organism gains entry to the submucosa of the stomach via a pre-existing ulcer. The patient presented in this communication might conceivably be an example of this.

The radiological appearance of gastric tuberculosis is very similar to that of neoplasia. Indeed, Gaines et al. (1952) felt that radiology had little to offer in arriving at a specific diagnosis of gastric tuberculosis. Our case supports this opinion.

Aird (1958) stated that gastric tuberculosis may rarely be the seat of a carcinoma, and Rentschler and Travis (1934) reported a case of gastric tuberculosis with a sarcoma. In the patient presented here there

---

* The General Infirmary, Leeds.

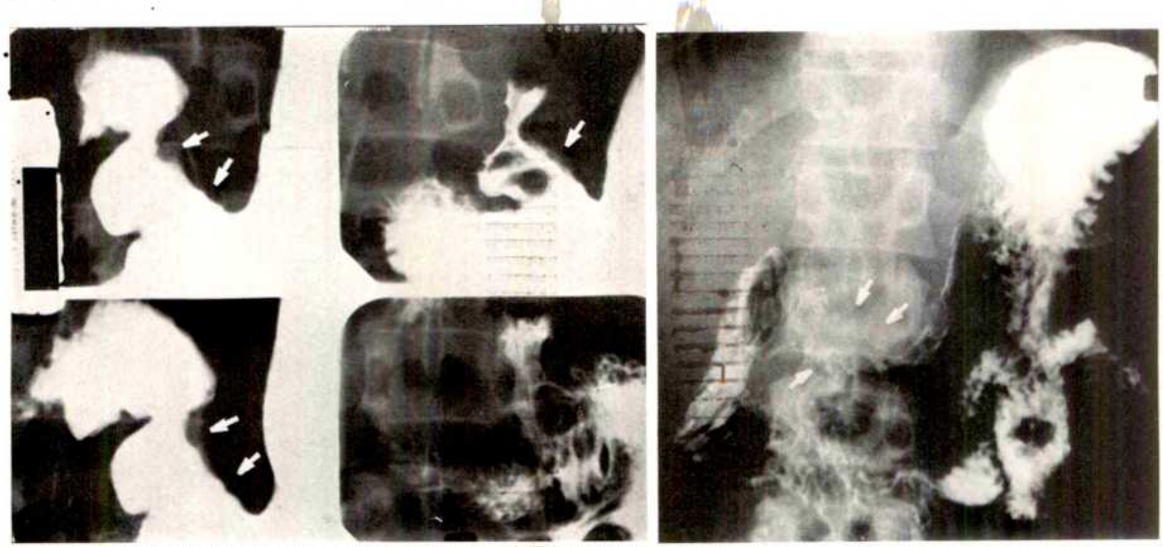


Fig. 1. Barium meal films showing a filling deformity in the antral region (arrows).

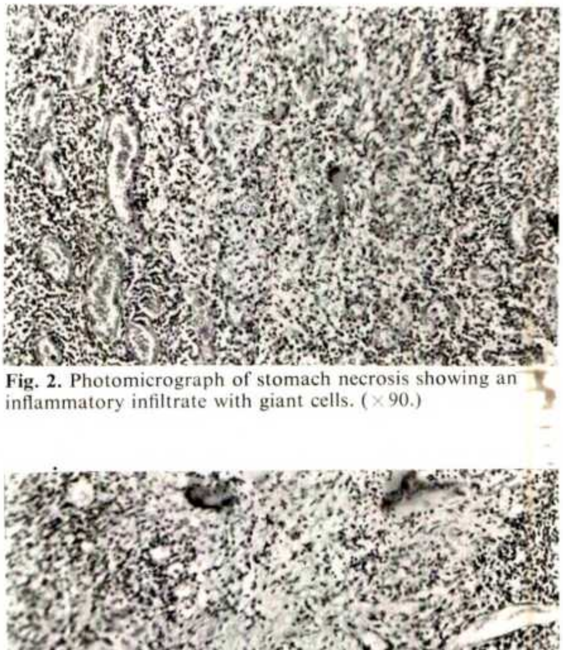


Fig. 2. Photomicrograph of stomach necrosis showing an inflammatory infiltrate with giant cells. (× 90.)

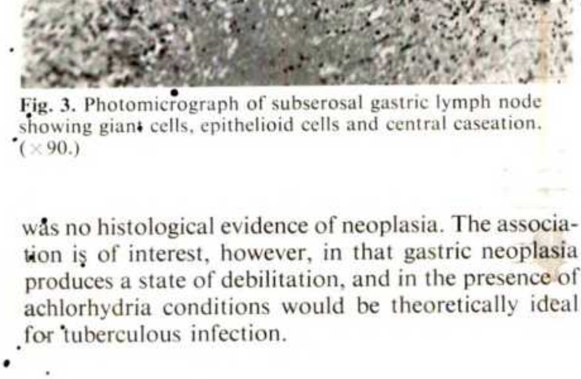


Fig. 3. Photomicrograph of subserosal gastric lymph node showing giant cells, epithelioid cells and central caseation. (× 90.)

was no histological evidence of neoplasia. The association is of interest, however, in that gastric neoplasia produces a state of debilitation, and in the presence of achlorhydria conditions would be theoretically ideal for tuberculous infection.

Stirk (1968) suggested treatment by partial gastrectomy where the lesion exists as a solitary ulcer. This procedure was followed, with success, in our patient. A course of anti-tuberculous drugs should be commenced as soon as the diagnosis is made, otherwise complications may ensue (Iles and Emerson, 1974).

References

ABRAMS J. S. and HOLDEN W. D. (1964) Tuberculosis of the gastro-intestinal tract. *Arch. Surg.* **89**, 282–293.

AIRD I. (1958) *A Companion in Surgical Studies*, 2nd ed. Edinburgh, Livingstone, p. 745.

GAINES W., STEINBACH H. L. and LOWENHAUPT E. (1952) Tuberculosis of the stomach. *Radiology* **58**, 808–818.

GOOD R. W. (1931) Tuberculosis of stomach; analysis of cases recently reviewed. *Arch. Surg.* **22**, 415–425.

GREENWOOD N. and FOX H. (1973) A comparison of methods for staining tubercle bacilli in histological sections. *J. Clin. Pathol.* **26**, 253–257.

HAMANDI W. J. and THAMER M. A. (1965) Tuberculosis of the bowel in Iraq: a study of 86 cases. *Dis. Colon Rectum* **8**, 158–164.

ILES P. B. and EMERSON P. A. (1974) Tuberculous lymphadenitis. *Br. Med. J.* **1**, 143–145.

KOSSICK P. (1969) Gastric tuberculosis. *S. Afr. Med. J.* **43**, 18–20.

KUZIONOV P. V. and POLINKOVA G. A. (1973) Multiple perforations of T.B. stomach ulcers. *Vestn Khir.* **110**, 134–135.

NOVIS B. H., BANK S. and MARKS I. N. (1973) Gastrointestinal and peritoneal tuberculosis. *S. Afr. Med. J.* **47**, 365–372.

PALMER E. D. (1950) Tuberculosis of stomach and stomach in tuberculosis; review with particular reference to gross pathology and gastroscopic diagnosis. *Am. Rev. Tuberc. Pulm. Dis.* **61**, 116–130.

RENTSCHLER C. B. and TRAVIS R. C. (1934) Sarcoma and tuberculosis of the stomach. *JAMA* **102**, 686–688.

STIRK D. I. (1968) Primary tuberculosis of the stomach, caecum, and appendix treated with anti-tuberculus drugs. *Br. J. Surg.* **55**, 230–235.

WALTER J. B. and ISRAEL M. S. (1974) *General Pathology*, 4th ed. Edinburgh, Churchill Livingstone. p. 243.

WIG K. L., CHITKAVA N. L., GUPTA P. S., KISHORE K. and MANCHANDA R. L. (1961) Ileocaecal tuberculosis with particular reference to isolation of *Mycobacterium tuberculosis. Am. Rev. Resp. Dis.* **24**, 169–178.

DISPRAY I
Trade Mark
Quick Prep
Chlorhexidine gluconate 0.5% w/v in 70% I.M.S.
Stuart Pharmaceuticals Limited Cheadle, Cheshire.
DISPRAY 2
Trade Mark
Hard Surface Disinfectant
Chlorhexidine gluconate 0.02% w/v in 70% I.M.S.
Stuart Pharmaceuticals Ltd Cheadle, Cheshire.

DISPRAY I
TRADE MARK
Quick Prep

Chlorhexidine Gluconate 0.5% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch
for skin disinfection

'Dispray' 1 Quick Prep.
(formerly known as Hibispray 1)
is an ideal preparation for skin and
hand disinfection in the busy
hospital environment.
At the touch of a button it gives
fast, easy and economical
skin disinfection prior to surgery,
injection or venepuncture.
When colour delineation
is required eg. pre-operatively,
'Dispray' 3 is available
with a red dye.

The 'Dispray' range
combines effectiveness with
convenience and economy.

Instant Availability.
No solutions to prepare.

Easy to use.
No swabs or bottles required.

Quick and Effective.
Rapid bactericidal action.

Efficient Application.
No wasted solutions.

Contents cannot
be contaminated.
No rejected solutions.

Long Lasting.
Contents of one can treat 100 sq. ft.

'Dispray' 1, 2, 3.
The Pick of the Bunch
for Disinfection.

DISPRAY 2
TRADE MARK
Hard Surface
Disinfectant

Chlorhexidine Gluconate 0.02% w/v
in 70% Industrial Methylated Spirit.

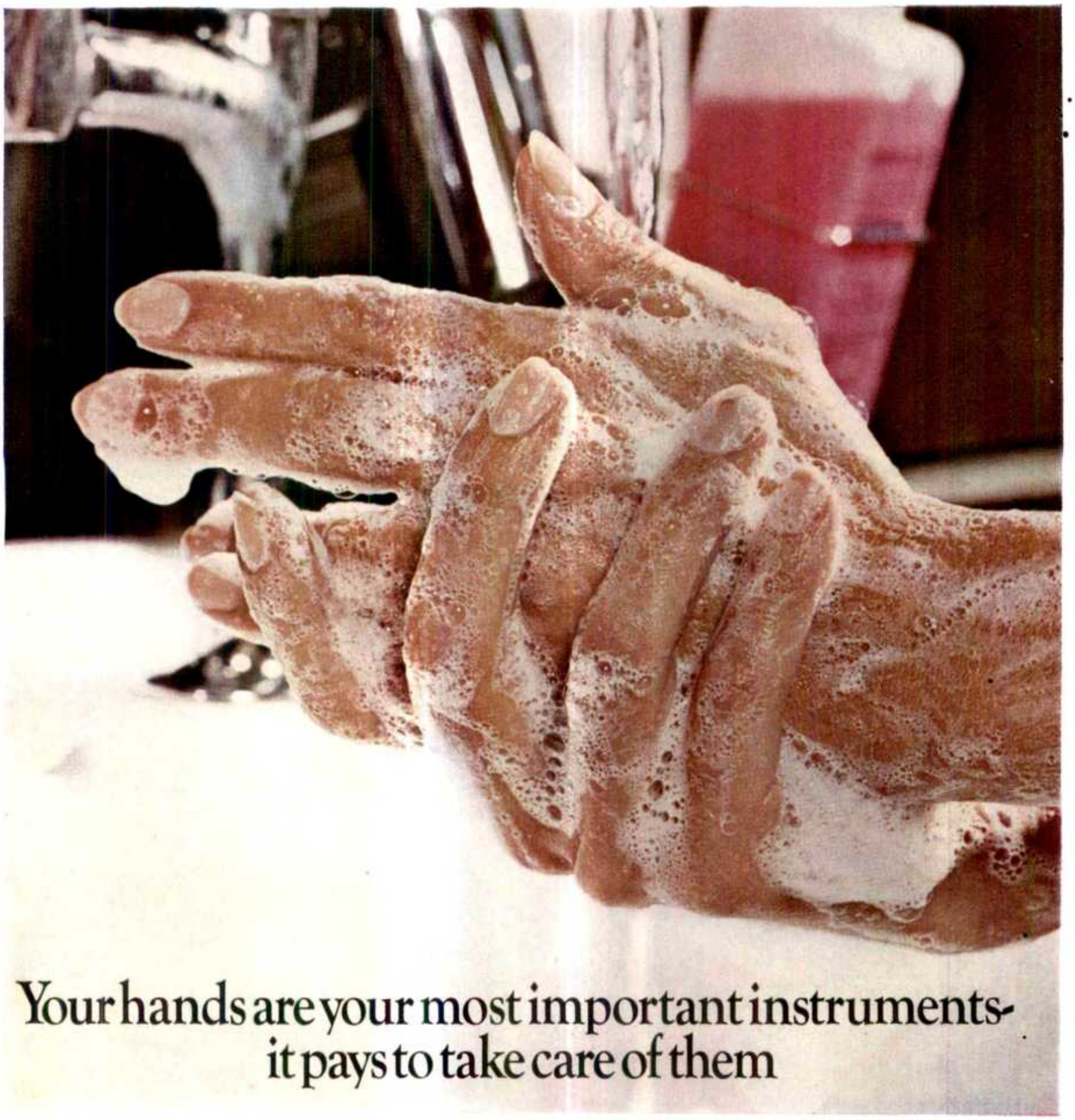
The pick of the bunch
for hard surface
disinfection

'Dispray' 2 Hard Surface
Disinfectant (formerly known as
Hibispray 2) provides rapid
disinfection of all hard surfaces
throughout the hospital.
Trolleys, cabinets, cupboards,
working surfaces – even footwear,
are rapidly, effectively
and efficiently disinfected.

Further
information
is available
from:

STUART

Stuart
Pharmaceuticals
Limited,
Carr House,
Carrs Road,
Cheadle,
Cheshire SK8 2EG.



Your hands are your most important instruments-it pays to take care of them

The obvious fact that a surgeon's hands are of prime importance to his work was borne in mind when 'Hibiscrub' was formulated. 'Hibiscrub' is designed to keep hands healthy, even after repeated use.

However, the prime importance of a handwash is effectiveness: rapid prolonged bactericidal action against skin bacteria is assured by the presence of the well-proven antiseptic 'Hibitane'.

"These studies have shown that a 4% chlorhexidine detergent solution ['Hibiscrub'] is a potentially outstanding addition to the small list of detergent-disinfectant preparations for the hands of surgeons and nurses, with a greater immediate effect than that obtained with the hexachlorophane or even the iodophor preparations."
British Medical Journal, (1973), 1, 510.

hibiscrub

RAPID BACTERICIDAL SKIN CLEANSER

Contains 'Hibitane' Chlorhexidine Gluconate 4% w/v.

ICI Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

'Hibitane' and 'Hibiscrub' are trade marks.

PH828

Br. J. Surg. Vol. 62 (1975) 621–623

Congenital hepatic fibrosis: aspects of diagnosis and surgical management

G. S. SOKHI, J. J. MORRICE, J. O'D. McGEE AND L. H. BLUMGART*

SUMMARY

Five cases of congenital hepatic fibrosis are described. In all the patients the diagnosis was delayed as a result of either failure to perform liver biopsy or misinterpretation of the histological features. Four patients had multiple operations for the control of haematemesis or the relief of portal hypertension. It is stressed that a high index of suspicion, the use of endoscopy and a liver biopsy are essential to avoid delay in diagnosis. The patients have a good prognosis provided that the diagnosis is established at an early stage and portacaval anastomosis performed.

CONGENITAL hepatic fibrosis was a term introduced by Kerr et al. (1961) to describe a condition occurring in children and young adults characterized by normal liver function, portal hypertension, hepatic fibrosis and preservation of the normal lobular liver architecture. Although the condition was first described by MacMahon in 1929, its clinical significance was not fully appreciated until recent years. Since the normal liver architecture and function are preserved the prognosis is good provided that the predominant clinical manifestation, portal hypertension, is treated adequately. This disease, however, is frequently diagnosed late and proper management is consequently delayed (Hermann and Hawk, 1967).

This paper presents 5 cases of congenital hepatic fibrosis which illustrate the difficulties in the clinical management. These patients, 3 of whom were personally managed, were encountered among 60 patients who underwent portasystemic shunt operations for the relief of portal hypertension during the years 1956–74 at the Glasgow Royal Infirmary.

Case reports

Case 1: A female child presented at the age of 1 year with haematemesis and melaena following ingestion of junior aspirin. There was no family history of haemorrhagic diathesis, congenital hepatic fibrosis or other hepatic pathology. On clinical examination the spleen and the liver were enlarged, but liver function tests were normal (*Table I*). Barium swallow studies showed no abnormality, and a diagnosis of Banti's syndrome was made. Liver biopsy was not performed. The patient was treated conservatively and discharged.

Three years later she again presented with haematemesis, and a barium swallow examination on this occasion showed oesophageal varices. She was treated by ligation of the splenic artery following which the spleen diminished considerably in size. Again liver biopsy was not performed and the diagnosis remained obscure.

Following this she remained well for a further 10 years, when she presented with iron deficiency anaemia, the haemoglobin being 11·1 g/100 ml. The packed cell volume was 37 per cent, white cell count 19 000/mm³ and platelets 248 000/mm³. The liver function tests were again normal and direct Coombs' test was negative. She was treated with oral iron therapy and discharged from hospital but without a firm diagnosis.

At the age of 17 the patient was admitted with massive haematemesis. She was treated by blood transfusion and intravenous vasopressin but without success. She continued to bleed, and direct transthoracic ligation of the gastro-oesophageal varices was carried out. Liver biopsy was performed at this time and a diagnosis of congenital hepatic fibrosis was made (*Fig*. 1). Intravenous pyelography revealed some fullness of the calices of the left kidney but no evidence of polycystic disease.

The patient had two further episodes of haematemesis in the following 2 years and another laparotomy was performed. The portal vein was found to be thrombosed and thrombectomy of the portal vein and a portacaval anastomosis was attempted.

Two years later she presented with a further gastro-intestinal haemorrhage. Oesophagogastroscopy demonstrated prominent varices in the oesophagus and the fundal region of the stomach. Liver function tests were again normal, the bilirubin being 0·8 mg/100 ml, SGOT 69·4 i.u./l, SGPT 21 i.u./l and alkaline phosphatase 6 KA units. At this point in her history she came under our care and a mesocaval shunt was carried out. The patient made an uneventful postoperative recovery and has been followed up for a year since the operation. Oesophagogastroscopy has been carried out at regular intervals and there has been diminution in the size of the varices. She remains well and has had no further bleeding. She has gained weight and is now working full time at a supermarket.

Case 2: This patient had a family history of congenital hepatic fibrosis and has been previously reported (Lorimer et al., 1967). She was remarkably healthy as a child but later in her life had multiple miscarriages. In 1964 at the age of 30 years she was admitted to hospital following an episode of haematemesis and melaena which was treated with blood transfusion and bed rest, but no definitive diagnosis was made. A year later she had two further episodes of gastro-intestinal bleeding, and more extensive investigations were undertaken. Clinically she appeared normal with no jaundice and no hepatosplenomegaly. A barium meal examination was carried out and oesophageal varices and a duodenal ulcer were demonstrated. Intravenous pyelography showed no abnormality. Liver function tests were within the normal range (*Table I*) and her bromsulphthalein excretion test showed 15 per cent retention at 30 minutes. Thrombotest was 45 per cent, direct Coombs' test was negative and serum copper oxidase and caeruloplasmin levels were also normal. The patient was slightly anaemic with a haemoglobin of 11·3 g/100 ml, packed cell volume of 32 per cent and platelet count of 50 000/mm³. Needle biopsy of the liver showed normal hepatic architecture intersected by a thick band of cellular fibrous tissue. At laparotomy the spleen was enlarged and the liver showed a 'fine cirrhosis'. The splenic pulp pressure was 36 cm H_2O and an operative portal venogram revealed a patent portal vein. Splenectomy and splenorenal anastomosis were carried out with a fall in the splenic pulp pressure to 24 cm H_2O. Liver biopsy obtained at operation showed the typical features of congenital hepatic fibrosis.

She remained well for 7 years following operation but was then readmitted with haematemesis. A duodenal ulcer was demonstrated on barium meal examination and a gastroenterostomy was therefore performed. She remained symptom-free for 2 years and was then admitted under our care with further haematemesis. She was not jaundiced but had definite

---

* University Departments of Surgery and Pathology, Glasgow Royal Infirmary.

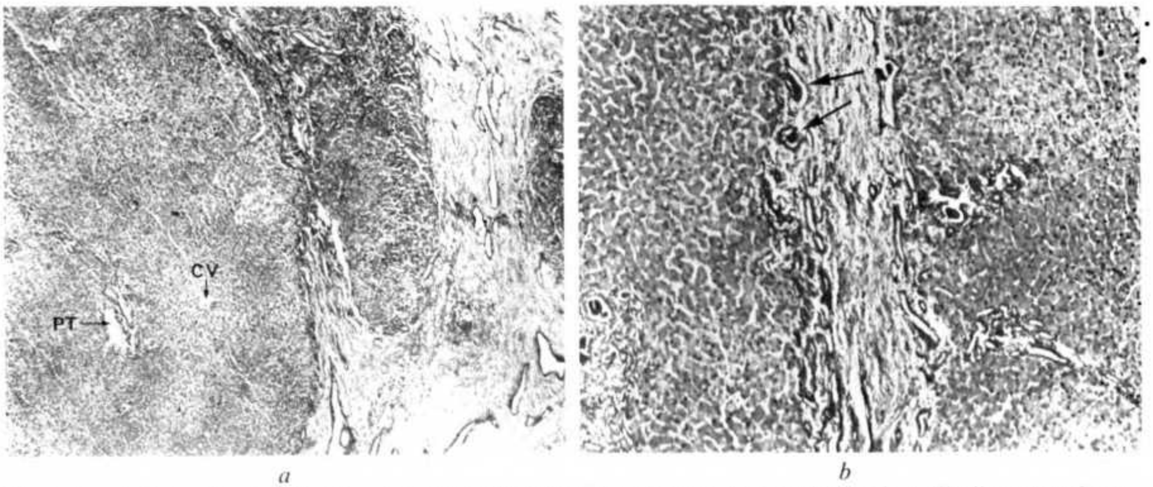


Fig. 1. *Case* 1. Wedge biopsy of the liver showing the typical features of congenital hepatic fibrosis. *a*, The liver parenchyma is transected by a thick band of collagen containing numerous large and medium-sized bile ducts. Note, however, that the basic architecture of the liver is normal, in that central veins (*CV*) and portal tracts (*PT*) bear a normal relationship to each other. (× 30.) *b*, Higher power view showing that the increase in number of medium-sized bile ducts occurs at the junction of the hepatic parenchyma and connective tissue septa. Note also inspissated bile in many of these ducts (arrows). (× 66.)

Table I: LIVER FUNCTION TESTS

Case	Total protein (g/l)	Albumin (g/l)	Globulin (g/l)	Bilirubin (mg/100 ml)	Alkaline phosphatase (KA units)	SGOT (i.u./l)	SGPT (i.u./l)
1	7·1	4·6	2·5	0·8	14·0	30	42
2	7·4	4·8	2·6	0·5	14·0	35	48
3	8·3	4·4	3·9	0·6	16·5	34	24
4	6·4	4·6	1·8	0·9	15·0	33	45
5	6·6	4·5	2·1	0·8	13·0	35	30

ascites. Liver function tests at this admission showed deterioration of hepatic function. The bromsulphthalein excretion test now showed retention of 50 per cent at 30 minutes, a bilirubin level of 1 mg/100 ml and alkaline phosphatase of 25 KA units. Oesophagogastroscopy showed prominent varices in the oesophagus and the cardiac region of the stomach. One of these varices was bleeding at the time of the endoscopic examination.

A mesocaval shunt was performed and the initial postoperative period was satisfactory. However, the patient then developed pulmonary oedema and bronchopneumonia. She became jaundiced and her condition progressively deteriorated. She died 19 days postoperatively. At post-mortem the liver was small and histology confirmed the diagnosis of congenital hepatic fibrosis. It also showed thrombosis of small hepatic venous radicles within the liver parenchyma. The mesocaval shunt was patent and the presence of bronchopneumonia was confirmed.

Case 3: This 60-year-old female patient was admitted with haematemesis. Oesophageal varices were demonstrated by barium swallow examination and a diagnosis of cirrhosis and portal hypertension was made. The liver function, however, was normal (*Table I*), the bilirubin being 0·8 mg/100 ml, SGOT 35 i.u./l, SGPT 30 i.u./l and alkaline phosphatase 13 KA units. Prothrombin time was also normal.

Splenoportography showed a patent portal vein and a portacaval anastomosis was performed. Biopsy of the liver was reported as showing atypical histological changes associated with cirrhosis of the liver, but the significance of the hepatic histology was not appreciated.

The patient was symptom-free for a year. She was readmitted with further haematemesis and was treated conservatively. A year later she presented again with gastro-intestinal haemorrhage and was managed by sedation, blood transfusion and intravenous administration of vasopressin. The haemorrhage, however, continued unabated and a Sengstaken tube was placed in the oesophagus. The patient's condition progressively deteriorated and she was transferred to our care.

The patient was semi-comatose, having had 12 units of blood transfused. A coagulation screen revealed an extrinsic clotting defect and thrombocytopenia, the platelets being 70 000/mm³ The liver function tests showed normal values of serum proteins, alkaline phosphatase and transaminases but the bilirubin was 10 mg/100 ml.

Splenoportography demonstrated an intact and patent porta vein, and there was no radiological evidence of portacaval shunt which was alleged to have been performed at a previous admission. Laparotomy was carried out and dense adhesions precluded dissection of the porta hepatis. Splenectomy and splenorenal shunt were performed and the liver biopsy confirmed the diagnosis of congenital hepatic fibrosis. Post operatively the patient developed hypotension, acute lef ventricular failure and anuria, and died 24 hours after operation. The post-mortem examination showed an intac splenorenal anastomosis but again no evidence of the portacaval shunt operation allegedly performed 2 years previously.

Case 4: A young boy aged 11 presented with haematemesis One year later he had a further attack and was noted to have hepatomegaly, but liver function tests were normal. Three year later he had a further episode of haematemesis and again live function tests were normal. During this admission his liver and spleen were both palpable. In view of the recurrent episodes o haemorrhage, splenectomy and splenorenal anastomosis were carried out. No liver biopsy was, however, performed.

The following year he had a further haematemesis and developed deep vein thrombosis. This presentation wa repeated 2 years later. He had three further episodes of haematemesis over the following 3 years and at that time, at the ag of 22, a further laparotomy was undertaken. The portal vei was found to be thrombosed and no definite operative procedure was undertaken. A liver biopsy demonstrated congenita hepatic fibrosis.

Four years later at the age of 26 he was readmitted, havin had five episodes of haematemesis and melaena. Liver functio tests were again normal (*Table I*). An oesophagogastrectom was performed but the patient collapsed and died on the second postoperative day.

Case 5: This male patient enjoyed good health until 1969 when, at the age of 29 years, he was admitted to hospital with haematemesis. Examination showed hepatosplenomegaly but the liver function tests were normal. His haemoglobin was 14·4 g/100 ml and platelets 36 000/mm^3. There was no family history of congenital hepatic fibrosis. He was submitted to laparotomy and the portal pressure was recorded as 32 cm H_2O. Splenectomy and a splenorenal anastomosis were carried out, and a diagnosis of congenital hepatic fibrosis was made on liver biopsy. His postoperative liver function tests showed little change from the preoperative findings. He has remained symptom-free since his operation and is now an active member of a parachute regiment.

Discussion

The aetiology of congenital hepatic fibrosis is not fully established but there is evidence that the condition is due to maldevelopment of the intrahepatic biliary system (Melnick, 1955). Familial incidence has been described (Lorimer et al., 1967; Campbell et al., 1958), and an autosomal recessive gene was incriminated by Kerr et al. (1961). The histological features are now well recognized (Nathan and Batsakis, 1969; Sommerchild et al., 1973): the lobular architecture of the liver is preserved but there is an increase in fibrous tissue and biliary ducts in the interlobular stroma (*Fig.* 1). Bile ducts may also be more numerous in otherwise normal portal tracts (Lorimer et al., 1967).

It is important that the correct diagnosis be established at an early date so that appropriate treatment can be instituted. These patients usually present with gastro-intestinal bleeding from oesophageal varices and have normal liver function, in contrast to patients with cirrhosis. The liver may be enlarged and splenomegaly is frequent. Splenoportography shows portal hypertension and a patent portal vein, suggesting an intrahepatic rather than an extrahepatic cause for the portal hypertension. Cystic anomaly of the kidneys demonstrated by intravenous pyelography adds further weight to the diagnosis of congenital hepatic fibrosis. Renal function, however, is usually normal. Percutaneous liver biopsy may be difficult to perform owing to the hard consistency of the liver, but biopsy with a Trucut needle (Travenol Laboratories Inc., Illinois, USA) provides connective tissue as well as parenchymal evidence and usually gives an adequate core, allowing accurate histological examination.

The prognosis is good provided that portal hypertension is corrected early in the course of the illness. However, owing to failure to perform a liver biopsy the diagnosis is often delayed, and as a result the patients undergo multiple inadequate operative procedures. This pattern is well illustrated by 3 of the cases described here (*Cases* 1, 2 and 4). The patients were treated at various hospitals for a number of years before liver biopsy gave the diagnosis and definitive portal decompression could be carried out.

The normal liver function and a patent portal vein make these patients excellent candidates for a portasystemic shunt with little risk of encephalopathy. The ideal operation is end-to-side portacaval anastomosis, but in very young children the procedure may be difficult. However, successful portacaval shunts can be performed after the age of 6 years (Hermann and Hawk, 1967). It has been recommended that an elective portasystemic shunt be performed in symptom-free patients with established portal hypertension due to congenital hepatic fibrosis (Sommerchild et al., 1973), and we would endorse this view. It is preferable to avoid splenectomy unless combined with splenorenal shunt as this may lead to thrombosis of the splenic or even the portal vein and so make further surgery difficult. This is well illustrated in *Cases* 1 and 4.

It is to be emphasized that these patients have a good chance of a normal lifespan if correct treatment is instituted at an early stage. A high index of suspicion, especially in young children or adolescents with haematemesis, the use of endoscopy in defining the site of haemorrhage, liver biopsy and adequate portasystemic shunt operation at the earliest opportunity are essential principles in the management of these patients. Our experience, like that of Kerr et al. (1961), indicates that the best results can be expected from early portacaval anastomosis.

References

CAMPBELL G. S., BICK H. D., PAULSEN E. P., LOBER P. H., WATSON C. J. and VARCO R. L. (1958) Bleeding oesophageal varices with polycystic liver: report of three cases. *New Engl. J. Med.* **259**, 904–910.

HERMANN R. E. and HAWK W. A. (1967) Congenital hepatic fibrosis as a cause of portal hypertension: report of two cases. *Surgery* **62**, 1095–1099.

KERR D. N. S., HARRISON C. V., SHERLOCK S. and WALKER R. M. (1961) Congenital hepatic fibrosis. *Q. J. Med.* **30**, 91–117.

LORIMER A. R., MCGEE J. and MCALPINE S. G. (1967) Congenital hepatic fibrosis. *Postgrad. Med. J.* **43**, 770–773.

MACMAHON H. E. (1929) Congenital anomalies of the liver. *Am. J. Pathol.* **5**, 499–508.

MELNICK P. J. (1955) Polycystic liver: analyses of seventy cases. *Arch. Pathol.* **59**, 162–172.

NATHAN M. and BATSAKIS J. G. (1969) Congenital hepatic fibrosis. *Surg. Obstet. Gynecol.* **128**, 1033–1041.

SOMMERCHILD H. C., LANGMARK F. and MAURSETH K. (1973) Congenital hepatic fibrosis: report of two new cases and review of the literature. *Surgery* **73**, 53–58.

Br. J. Surg. Vol. 62 (1975) 624–628

Splenic-gonadal fusion

A. K. PENDSE, P. N. MATHUR, M. M. SHARMA AND O. P. GUPTA*

SUMMARY

Various aspects of splenic-gonadal fusion are discussed and 1 case of the continuous type is reported. A plea is made to include this condition in the differential diagnosis of scrotal masses, particularly those on the left side.

SPLENIC-GONADAL fusion, manifesting as abnormal connections between the spleen and the left gonad or the derivatives of the left mesonephros, has been observed occasionally. Fifty-four cases of this anomaly had been reported up to 1969 (Mendez and Morrow, 1969). These masses, which invariably occur on the left side, are often taken to represent a third testicle or a testicular tumour. A case of splenic-gonadal fusion is presented and important aspects of this condition are reviewed in this paper.

Case report

G. C., aged 2½ years, was admitted with a history of left-sided scrotal swelling which had first been noticed by the parents about 6 months previously. The swelling tended to vary in size.

On examination a 5 × 3 cm swelling was palpable in the left scrotum. It was firm in consistency, and the testis and epididymis could not be palpated separately. The cord was slightly thickened. Trans-illumination was negative.

The left scrotum was explored under general anaesthesia. There was a congenital hernial sac with an unobliterated processus. The testis and the epididymis were elongated and did not show a normal configuration. On the lateral aspect of the testis and epididymis there was a 5 × 3-cm oblong mass with a broad lower end adjoining the globus major and tapering towards the upper end. From the tapering end and also from the testis a fibrous cord extended along the spermatic cord and disappeared beyond the internal inguinal ring. The mass was reddish-brown in colour and had a glistening capsule. It could not be dissected away from the testis and the epididymis. Because of this and the uncertainty about the nature of the mass, orchidectomy was carried out. The postoperative course of the patient was uneventful.

Gross examination confirmed the operative findings (*Figs.* 1, 2). Histological examination revealed histologically normal splenic, testicular and epididymal structures with a fibrous septum separating the two elements.

Discussion

Classification

There are two forms of the malformation:

1. *Continuous splenic-gonadal fusion* in which the spleen remains connected with the left gonad by a continuous strand of splenic tissue or by a fibrous cord containing accessory splenic islands at various levels. The cord usually arises from the upper pole of the spleen (Putschar and Manion, 1956), although it may arise from the hilum (Bennett-Jones and St. Hill, 1952) or from the lower pole (Daniel, 1957). The spleen is otherwise normally formed and located, but may be lobulated or fissured. The cord tapers from the

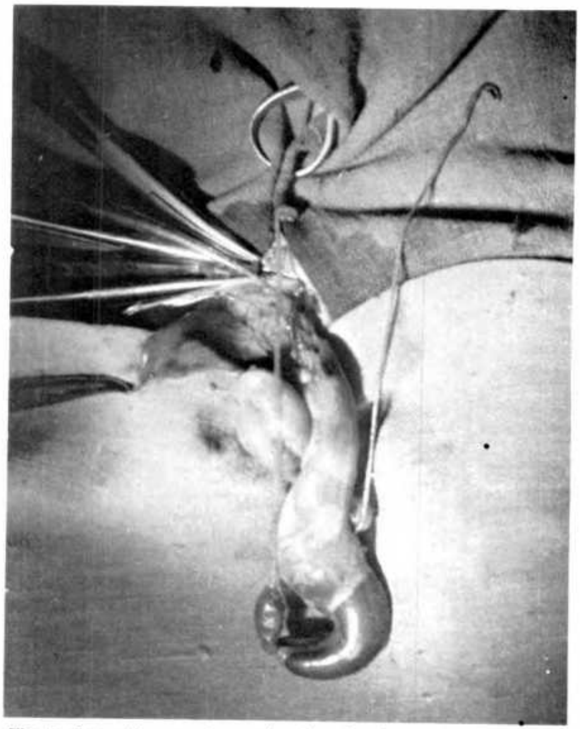


Fig. 1. Operation specimen showing the elongated testis and epididymis (upper pale structure) and curved tapering splenic tissue (lower dark structure). The two fibrous cords are also visible.

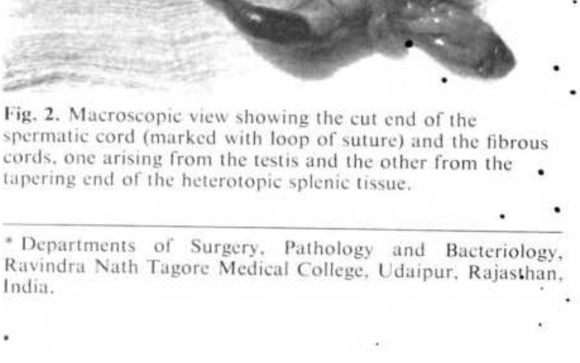


Fig. 2. Macroscopic view showing the cut end of the spermatic cord (marked with loop of suture) and the fibrous cords, one arising from the testis and the other from the tapering end of the heterotopic splenic tissue.

---

* Departments of Surgery, Pathology and Bacteriology, Ravindra Nath Tagore Medical College, Udaipur, Rajasthan, India.

spleen downwards, or is beaded with local aggregations of the splenic tissue, and often ends in a bulbous mass of spleen attached to the gonad (Willis, 1962). The cord traverses the peritoneal cavity as a free structure in front of the intestines, but may be paracolic.

2. *Discontinuous splenic-gonadal fusion* in which a mass of accessory splenic tissue is attached to the gonad, but there is no connecting cord between this and the spleen proper. The accessory paragonadal spleen is usually a distinct encapsulated mass attached to the testis or to the head of the epididymis. Occasionally there may be multiple masses.

Aetiology

Between the fifth and eighth embryonic weeks the developing splenic rudiment in the dorsal mesogastrium is in close relationship to the mesonephros and gonadal rudiment. Abnormal adhesion of the two rudiments, as most investigators assume (Putschar and Manion, 1956), or the development of splenic tissue from a wider field than normal, extending on to the dorsal coelomic wall (Willis, 1962), would account for caudal displacement of the part of the spleen in contact with the gonad when the latter descends. This explains the genesis of the continuous type of splenic-gonadal fusion. The less frequent discontinuous type of fusion may be derived from an isolated hump of the splenic anlage, or the original connection with the main spleen may disappear, leaving no vestiges.

Associated malformations

These have been present in approximately 20 per cent of the recorded cases and include peromelus, micrognathia, atresia of the anus, asymmetry of the skull and abnormal fissures of the lung and liver. Putschar and Manion (1956) point out the too frequent association of peromelus and micrognathia with splenic-gonadal fusion and suggest that these features may constitute a syndrome. The associated malformations have been reported exclusively in the continuous type of fusion. None of the reported discontinuous types showed any such malformations.

Gross and histological findings

The splenic tissue is only in close approximation with the gonad and usually no intermingling with the mesonephric-gonadal tissue is seen, though this has occasionally been reported (Bennett-Jones and St. Hill, 1952).

The splenic tissue of the cord as well as of the isolated aberrant spleen is histologically normal, but may show regressive changes such as fibrosis, thrombosis, calcification, thickening of the trabeculae and deposition of blood pigment. The splenic tissue may participate in the function of the main spleen and show hyperplasia (Emmett and Dreyfuss, 1943). It is also subject to the same pathological conditions as the main spleen.

The area of fusion with the gonad is variously described as a thinned or thickened layer of fibrous tissue. The gonad is usually normal histologically but may show atrophy, fibrosis and an increased number of Leydig cells (Talmann, 1926; Tate and Goforth, 1949).

Clinical considerations

The sex distribution of this congenital anomaly strongly favours the male, especially in the continuous type of fusion.

The left gonad is almost exclusively involved; only 1 case of right scrotal spleen has been reported.

The aberrant splenic tissue is usually found accidentally during hernial repair, operation for undescended testicle or at necropsy. The splenic tissue may present as a scrotal mass or masses and is then taken to represent a third testicle (Daniel, 1957) or is confused with a testicular tumour (Horovitz and Griffel, 1959; Mendez and Morrow, 1969). Pain and tenderness, particularly during strenuous exercise, may force the patient to seek medical advice. Enlargement of the mass during systemic infections and malaria has also been reported. Accessory splenic tissue must be considered in the differential diagnosis of scrotal masses, especially on the left side.

The abnormal fusion of the spleen to the mesonephric-gonadal structures frequently interferes with the normal completion of gonadal descent and the orderly closure of the processus vaginalis. Of the 54 reported cases, 17 had an associated inguinal hernia and 9 had incomplete gonadal descent (Mendez and Morrow, 1969).

Splenic-gonadal fusion *per se* does not require any treatment. The heterotopic splenic tissue is usually revealed during exploration of a scrotal mass and, unless one is aware of this anomaly, orchidectomy is carried out, as was done in our case. Repeated attacks of pain and swelling, specially in the presence of an atrophic testicle, necessitate orchidectomy. Excision of the heterotopic splenic tissue is indicated when it participates in diseases involving the spleen (leukaemia, infectious mononucleosis, etc.), or when its continued presence results in failure of splenectomy in cases of thrombocytopenic purpura and acholuric jaundice. The splenic-fibrous band stretching from the spleen to the internal inguinal ring may cause mechanical intestinal obstruction (Hines and Eggum, 1961).

Appendix: Review of reported cases

Fifty-four cases of splenic-gonadal fusion have been reported in the literature. The details of clinical presentation and gross and microscopic features are available for 37 of the cases and are given in *Table I*. A review of the reported cases shows a marked preponderance of males—50 males and 4 females. The continuous type of splenic-gonadal fusion (type I) was present in 25 cases, the discontinuous type (type II) in 23 cases while the type was not specified in 6 cases. Inguinal hernia was reported to be present in 18 cases, absent in 20 cases and was not specifically mentioned in 16 cases. Incomplete descent of the fused gonadal-splenic structure was present in 9 cases,

Table I: DETAILS OF THE REPORTED CASES

Authors	Sex (age, yr)*	Clinical diagnosis	Type (side)†	Gross anatomy	Histology/Associated anomalies‡
1	M (n.g.)	No details	I (l.)	Fusion, with normal location of both organs	No details
2	M (n.b.)	No details	I (l.)	Cord 5·5 cm long, 3·5–6 mm wide. Testes undescended	No details *Perobrachius apus, micrognathia, anal atresia and defect of coccyx*
3	M (n.g.)	No details	I (l.)	No details	No details *Not mentioned*
4	M (a.)	Third testicle	I (l.)	Nodule 2 × 1 cm. Cord 33·4 cm long, 1–10 mm wide	Histologically normal spleen *Not mentioned*
5	M (25)	Inguinal hernia	I (l.)	Nodule 2·5 cm. Cord 43 cm long	Histologically normal spleen *Not mentioned*
6	M (10)	Death due to typhoid	I (l.)	Both testicles at external ring	Hypoplastic testes *Absence of left lower leg*
7	M (n.b.)	Inguinal hernia	II (l.)	Spleen in left epididymis	No details *Not mentioned*
8	M (22)	Tenderness and swelling of the left testicle after long marches and during malaria	II (l.)	Mass 2·5 cm in the head of the epididymis and another on the spermatic cord	Atrophic testicle, splenic hyperplasia *Not mentioned*
9	M (19)	Exploration at age of 12 for scrotal mass	II (l.)	Three masses at the lower pole of testis	Atrophic changes in the testis. Normal splenic tissue *Not mentioned*
10	F (n.b.)	No details	I (l.)	Cord 77 mm long, 0·5–2·5 mm wide	No details *Not mentioned*
11	M (11)	Found during operation for undescended testicle	I (l.)	Cord 2 mm wide	Histologically normal spleen *Not mentioned*
12	M (n.g.)	Tertian malaria with painful swelling of the scrotal spleen	II (l.)	No details	No details *Not mentioned*
13	M (30)	Exploration at age of 12 for scrotal mass	II (l.)	Three masses at the lower pole of testis	Atrophic changes in the testicle, normal spleen *Not mentioned*
14	M (19)	Congenital left inguinal hernia with aberrant spleen	I (l.)	Pear-shaped mass 4·6 × 2·2 × 1·5 cm. Cord 9 cm long	Histologically normal spleen *Not mentioned*
15	M (43)	Bilateral inguinal hernia with tumour of left testicle	II (l.)	Mass 4 × 2 cm at the upper pole of testis	Histologically normal splenic and testicular tissue *Not mentioned*
16	M (45)	Cause of death: peritonitis from perforated bleeding duodenal ulcer	I (l.)	Spleen 200 g, normal position. Cord 0·3–0·5 cm wide. Ectopic spleen 1·8 × 1 × 1 cm as bulbous mass at head of epididymis	Splenic tissue with inflammatory hyperplasia *Not mentioned*
17	M (32)	Pain in left testicle and scrotum. Mass noticed since birth. Discomfort after exercise	I (l.)	Marble-sized splenic tissue at lower end of left spermatic cord. Cord 12 cm long followed only up to internal ring	Normal splenic tissue *Not mentioned*
18	M (9)	Found during medical inspection at school	II (l.)	Walnut-sized accessory spleen at inferior pole of testicle	Histologically normal spleen *Not mentioned*
19	M (21)	Swelling noticed at age of 13, after operation for undescended testicle	I (l.)	Mass 7 × 4 × 4 cm attached to atrophic left testicle. Tail-like process along spermatic cord, 10 cm long, followed up to inguinal ring	Normal splenic tissue. Atrophic testis without spermatogenesis, increased fibrous tissue and Leydig's cells *Not mentioned*
20	M (9)	On palpation of heavy right testicle, five times normal size with irregular bosselated surface. Diagnosis: malignant tumour	II (r.)	Specimen showed semi-lunar-shaped testicle in upper third and firm, reddish nodular splenic mass in lower two-thirds	Normal spleen and immature testis *Not mentioned*
21	M (4)	Noted at physical examination for cardiac malformation	II (l.)	Accessory spleen 3 × 5 × 2 cm in upper pole of left testicle	Histologically normal spleen and testicle *Patent ductus arteriosus*
22	M (69)	Cause of death: fall from tree, rupture of aorta and mediastinal haemorrhage	I (l.)	Bilobed spleen with a beaded cord from lower pole to 2-cm splenic mass in upper pole of left testis	Normal spleen with considerable free pigment *Not mentioned*
23	M (13)	Left testicle larger than right since birth, painful on effort—malignant tumour	II (l.)	Splenic mass 8 × 4 × 3 cm at upper pole of left testis	Spleen with hyalinization of arterioles *Not mentioned*
24	M (10)	Seen at 7 years because of tender enlarged testis. Diagnosis: partial torsion or thrombosis of spermatic cord	I (l.)	Cord 20 cm long, 0·6–1·2 cm wide. Little macroscopic demarcation between cord and splenic mass	Histologically normal spleen *Not mentioned*

25	F (n.b. probably)	No details	I (l.)	Splenic cord from upper pole of left spleen to slightly undescended left ovary. Two intra-ovarian splenic nodules	No details *Thoracopagus, single jejunum and ileum, Meckel's diverticulum and vascular anomalies*
26	M (6/12)	Cause of death: bronchopneumonia	I (l.)	Medium-sized spleen 5 cm. Splenic process from upper pole continuing as 7-cm long fibrous cord inserted at left innominate line. Both normal testicles in scrotum	No details *Peromelus, micrognathia, absence of both forearms and legs, abnormal fissures of lungs and liver, asymmetry of skull*
27	F (s.b.)		I (l.)	Spleen 6 × 2·3 cm, normal position. Elongated process from upper pole, 0·5 cm wide at lower end, attached to partly undescended left adnexa. Tubes, ovaries and uterus normal	Normal congested splenic tissue. Splenic cyst with capsule-like wall *Micrognathia, absence of both forearms and hands, absence of right lower leg and foot*
28	M (24)	Recurrent attacks of epididymitis and inflammation of spermatic cord following herniorrhaphy several years previously	II (l.)	Accessory spleen 4·5 × 2 × 1 cm with smooth grey capsule, located in upper part of left testicle	Splenic tissue with some fibrosis of stroma and reduced pulp *Not mentioned*
29	M (23)	Mass in scrotum since 1945. Recent increase in size, without symptoms	II (l.)	Accessory spleen 1·7 × 2·3 cm in upper pole of left testis, completely encapsulated testis; epididymis and vas normal. Dilatation of pampiniform plexus	Histologically normal splenic tissue *Not mentioned*
30	M (11)	Tumour of scrotum	II (l.)	Mass 1·5 × 1·4 × 1·1 cm, encapsulated, ovoid, smooth, deep red surface; cut surface greyish-pink in soft tissue between scrotal skin and spermatic cord	Well-defined capsule with many lymphoid follicles, elongated sinusoidal spaces lined by endothelium *Not mentioned*
31	M (44)	Pain and swelling in lump in left scrotum for 15 mth. Lump noticed at age of 8. Exploration at 21 yr	I (l.)	Small nodule of splenic tissue, red-brown in colour, in upper pole of left testis, but separate from it. Cord not traced but palpable clinically up to external ring	Histologically normal spleen *Not mentioned*
32	M (26)	Soreness and pain in third testicle, noticed since birth, and left inguinal hernia. Congenital tumour or duplication of left testis	I (l.)	Two masses, 2·3 × 3·5 cm, firm, solid, homogeneous brownish red, each with a cord 27 cm long, average diameter 0·75 cm	Normal spleen and testicle *Not mentioned*
33	M (5)	Soft, non-tender swelling in left scrotum, moving with testicle. Clinical diagnosis: hydrocele	II (l.)	Dark brown, well-encapsulated tumour 2·5 × 2 × 2 cm	Normal spleen and testicle *Not mentioned*
34	M (15)	Acute intestinal obstruction due to elongated projection of splenic tissue	I (l.)	Elongated projection of splenic tissue extending from lower end of bilobate spleen. Lower end fibrous, leaving abdomen through left inguinal ring. Testicular connection not traced	Not mentioned *Not mentioned*
35	M (32)	Swelling of left side of scrotum since childhood. Gradual increase in size, no pain. Clinical diagnosis: neoplasm of testis	II (l.)	Mass of tumour and testes 12 × 8 × 7 cm. Testis compressed at the lower pole of the tumour. Encapsulated, reddish brown splenic tissue	Congestive splenomegaly. Little atrophy of the compressed tubules with absent spermatogenesis in testis *Not mentioned*
36	F (48)	Nullipara with menorrhagia and double uterus	I (l.)	Mass 1·5 cm attached to left ovary	Not mentioned *Double uterus*
37	M (49)	Clinical diagnosis: epididymo-orchitis with embarrassed testicular blood supply. Hernioplasty on same side	II (l.)	Mass 10 × 8 × 7 cm, bright red. No evidence of testicular tissue, but with a dilated 3·5 × 4 cm cystic cavity	Fibrocongestive splenomegaly; dense fibrous connective and inflammatory tissue with abscess formation and foreign body granuloma *Not mentioned*

Authors—1: Bostrem (1883); 2: Pommer (1889); 3: Abbutt and Rolleston (1908); 4: Sneath (1913); 5: Heitzmann (1917); 6: Skworzoff (1924); 7: Finaly (1926); 8: Talman (1926; 9: Osseladore (1928); 10: Wiltschke (1929); 11: Fischer and Gissel (1935); 12: Settle (1940); 13: Frasson (1942); 14: Kadlic (1943); 15: Emmett and Dreyfuss (1943); 16: Olken (1945); 17: Andrews and Etter (1946); 18: Sartor (1948); 19: Tate and Goforth (1949); 20: Gordeef and Cuenant (1951); 21 and 22: Keizur (1952); 23: de Cesaris (1952); 24: Bennett-Jones and St. Hill (1952); 25: Von Hochstetter (1953); 26: Werthemann and Roulet (1954); 27–30: Putscher and Manion (1956); 31: Jayne and Jessiman (1955); 32: Daniel (1957); 33: Horovitz and Griffel (1959); 34: Hines and Eggum (1961); 35: Lynch and Kareim (1962); 36: Almenoff (1966); 37: Mendez and Morrow (1969). Authors not detailed in the reference list have been cited by Putschar and Manion (1956) or Mendez and Morrow (1969).

* n.g. = not given; n.b. = newborn; a. = adult; s.b. = stillborn.

† Type (side) = Type of fusion (side involved). l. = left. r. = right. Type I = continuous; II = discontinuous.

‡ Associated anomalies shown in italics.

absent in 36 cases, and was not specified in 9 cases. In all of the reported cases except one the anomaly affected the left gonad.

A correct preoperative diagnosis of scrotal spleen was made in only 1 of the 54 cases. Most of the cases were discovered at clinical examination for some other disease or during exploration for inguinal hernia or undescended gonads. The mass has often been confused with a scrotal/testicular neoplasm, a supernumerary testis or epididymo-orchitis. In 1 case the splenic-fibrous cord caused acute intestinal obstruction. The heterotopic splenic tissue has been reported to manifest changes similar to those occurring in the parent spleen.

Acknowledgements

The authors are grateful to the Principal and Controller, Ravindra Nath Tagore Medical College and Associated Group of Hospitals, Udaipur, Rajasthan, for permitting us to publish this paper.

References

BENNETT-JONES M. J. and ST. HILL C. A. (1952) Accessory spleen in the scrotum. *Br. J. Surg.* **40**, 259–262.

DANIEL D. S. (1957) An unusual case of ectopic splenic tissue resembling a third testicle. *Ann. Surg.* **145**, 960–962.

EMMETT J. M. and DREYFUSS M. L. (1943) Accessory spleen in the scrotum; review of literature on ectopic spleens and their associated surgical significance. *Ann. Surg.* **117**, 754–759.

HINES J. R. and EGGUM P. R. (1961) Splenic-gonadal fusion causing bowel obstruction. *Arch. Surg.* **83**, 887–889.

HOROVITZ L. and GRIFFEL B. (1959) Aberrant splenic tissue mistaken for hydrocoele. *Lancet* **2**, 442–443.

MENDEZ R. L. and MORROW J. L. (1969) Ectopic spleen simulating testicular tumour. *J. Urol.* **102**, 598.

PUTSCHAR W. J. and MANION W. C. (1956) Splenic-gonadal fusion. *Am. J. Pathol.* **32**, 15–33.

TALMANN I. M. (1926) Nebenmilzen in Nebenhoden und Samenstrang. *Virchows Arch.* (*Pathol. Anat.*) **259**, 237.

TATE G. W. and GOFORTH J. L. (1949) Accessory spleen in the scrotum—report of a case. *Texas St. J. Med.* **45**, 570–573.

WILLIS R. A. (1962) *The Borderland of Embryology and Pathology*, 2nd ed. London, Butterworths, pp. 334–335.

Br. J. Surg. Vol. 62 (1975) 629–632

Abdominoscrotal hydrocele

B. R. PAREKH, G. REINBOTH AND O. P. MISHRA*

SUMMARY

The number of cases of abdominoscrotal hydrocele reported in the literature has been brought up to date, which, including the 3 cases reported here, is 83 of which 21 are from India.

The pathogenesis of this lesion is discussed. It is concluded that all cases of abdominoscrotal hydrocele are due to progressive involvement and distension of the patent processus vaginalis which is cut off from the general peritoneal cavity.

A new classification of abdominoscrotal hydrocele is suggested on the basis of experience gained from the 3 cases reported here.

SINCE the first description by Dupuytren in 1834, who called this condition 'l' hydrocèle en bissac', numerous names have been suggested from time to time. Lister, who was interested by the extraordinary clinical appearance of a patient, did a post-mortem dissection of this lesion and published his results in 1856. Jacobson, whose classification of the types of hydrocele is still used today, described it as 'infantile hydrocele with prolongation into the abdomen' in his textbook published in 1893. However, it was Bickle in 1919 who suggested the term 'abdominoscrotal hydrocele' for this condition as a proper descriptive title, and although Holmes recommended the term 'properitoneal hydrocele' in 1932, the term 'abdominoscrotal hydrocele' is now generally used.

Abdominoscrotal hydrocele is considered a relatively rare condition, and most of the published reports are based on a single case. To the best of our knowledge the total number of cases reported in the literature to date is 80. These include 18 cases reported from India during the past 10 years, The present report is based on the experience of 3 cases, all young male Hindus, which bring the total of published cases to 83 including 21 from India.

Case reports

Case 1: M. L. M., aged 30 years, was admitted on 5 May 1959 with a gradually increasing swelling in the right side of the scrotum of 2 years' duration. The past history and family history were non-contributory. General and systemic examinations found nothing significant. Local examination revealed a right-sided, moderately large and tense, inguinoscrotal, cystic, translucent swelling in which a cough impulse was present. A clinical diagnosis of right-sided infantile hydrocele was made.

The patient underwent operation on 6 May (O. P. M.). Through an inguinal incision the distended processus vaginalis lying in the inguinal canal was dissected free from the spermatic cord and tapped to reduce the size of the scrotal part of the hydrocele, and then the scrotal part of the hydrocele with the testis was delivered into the inguinal canal. It was noted with surprise that the amount of straw-coloured hydrocele fluid collected in the suction bottle was obviously much more than what appeared to have been contained in the hydrocele sac. The sac was opened and a finger passed into the proximal part of the sac and negotiated through the internal inguinal ring where the lumen of the processus vaginalis was expected to be obliterated. However, a finger slipped in as it would in a hernial sac, but the loops of the intestine could not be felt in direct contact with finger. It was then realized that the condition was an abdominoscrotal hydrocele and the abdominal part of the hydrocele sac was lying in the properitoneal space deep to the fascia transversalis. With gentle and steady traction the whole of the abdominal part of the sac was pulled out through the internal ring. At this stage the obliterated communicating isthmus between the processus vaginalis and the peritoneal cavity came into clear view (*Fig.* 1). With gentle manipulation, a closed artery forceps was made to pass through this isthmus which was then stretched and a finger inserted into it. This finger came into direct contact with a loop of intestine. The isthmus was transfixed and divided and the proximal sac was excised by dividing the processus at the upper pole of the testis. The tunica vaginalis was everted and the testis returned into the scrotum. The incision was closed in layers.

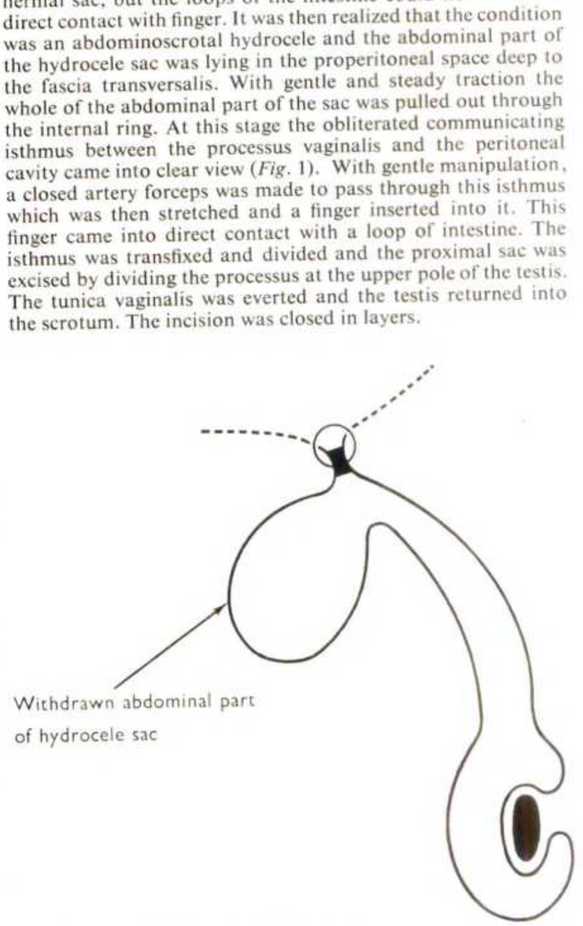


Fig. 1. *Case* 1. Diagram of the hydrocele.

Case 2: J. K. N., aged 20 years, presented on 17 February 1969, with a painful irreducible swelling in the right inguinal region. The patient had noticed a small swelling in this region about 1 month previously which was neither painful nor tender. He could not confirm or deny the reducibility of the swelling. The swelling had suddenly became painful about 20 hours before admission. The patient gave no history of distension of the abdomen and had passed a normal motion in the morning. General and systemic examinations revealed no abnormality. Locally, there was a swelling about 2·5 cm in diameter. The skin over the swelling was normal and moved freely. The swelling was cystic, tender and irreducible. A clinical diagnosis of strangulated omentocele was made and an emergency operation under spinal anaesthesia was performed (O. P. M.).

---

* Department of Surgery, Medical College, Jabalpur (MP), India.

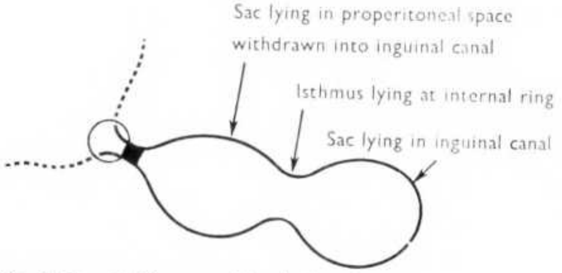

Sac lying in properitoneal space withdrawn into inguinal canal
Isthmus lying at internal ring
Sac lying in inguinal canal

Fig. 2. *Case* 2. Diagram of the hydrocele.

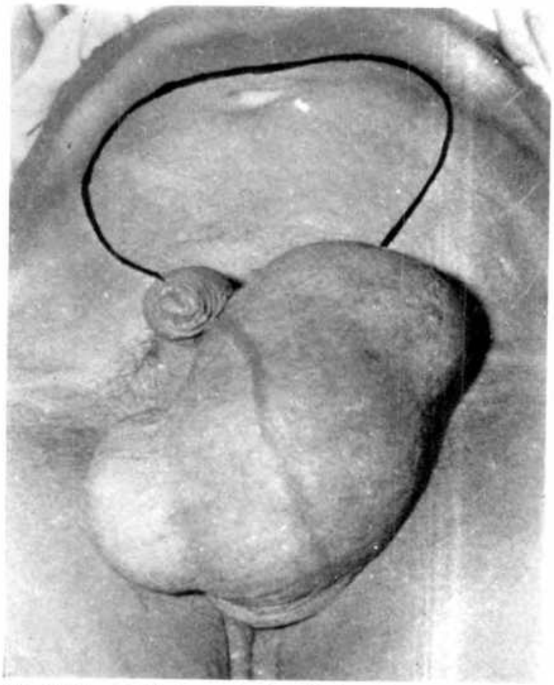


Fig. 3. *Case* 3. Photograph of the hydrocele. The cystic swelling in the abdomen is outlined.

Through an inguinal incision a thin-walled, tense, cystic swelling measuring 5 × 2·5 cm and containing clear straw-coloured fluid was seen lying in the inguinal canal and extending up to the internal inguinal ring; the appearances were of a high encysted hydrocele of the cord. There appeared to be no cause to explain the sudden pain and tenderness in the swelling, and hence it was presumed to be due to partial volvulus which had already been relieved either spontaneously or during the exposure and handling of the swelling. An attempt was made to separate the sac from the structures of the cord for excision, but during the dissection the cyst ruptured. At the extreme proximal end of the cyst a narrow processus communicating with the lumen of the cyst was found entering the internal inguinal ring. With gentle and steady traction the processus was pulled out, and was found to have dilated into a larger sac lying in the properitoneal space. The whole of the properitoneal part of the sac was easily brought out. This sac was attached to the parietal peritoneum by a narrow obliterated isthmus of the processus vaginalis (*Fig.* 2). As in *Case* 1, with gentle manipulation a closed artery forceps was made to pass through the isthmus in order to confirm the communication with the general peritoneal cavity, and then the isthmus was transfixed and the hydrocele sac was excised. The patient had an uneventful recovery and was discharged from hospital on 26 February.

Case 3: K. S., aged 25 years, was admitted on 13 April 1973 with a swelling in the left scrotum which had been gradually enlarging for the past 6 months. The past history and family history were non-contributory. No abnormality was detected on general and systemic examination. On local examination there was a moderately large, translucent, left-sided, vaginal hydrocele. A visible cough impulse was present. On further examination a fairly large cystic swelling was found in the abdomen, occupying the hypogastric region and part of the left lower abdomen and extending upwards beyond the umbilicus (*Fig.* 3). This swelling was dull on percussion and was non-tender, and the patient was unaware of its presence. The swelling became less prominent on contraction of the abdominal muscles, and was felt per rectum on being pressed down by a hand placed on the abdomen. Cross-fluctuation was present between the abdominal and scrotal swellings. A clinical diagnosis of abdominoscrotal hydrocele was made and the patient underwent operation on 28 April under spinal anaesthesia (O. P. M.).

The scrotal part of the hydrocele was exposed through a 6-cm scrotal incision placed 1 cm to the left and parallel to the median raphe. The sac was tapped through a wide bore needle connected to a suction machine in order to reduce its size, and the structures of the spermatic cord were separated from the sac at the upper part of the scrotum. Then, with gentle and

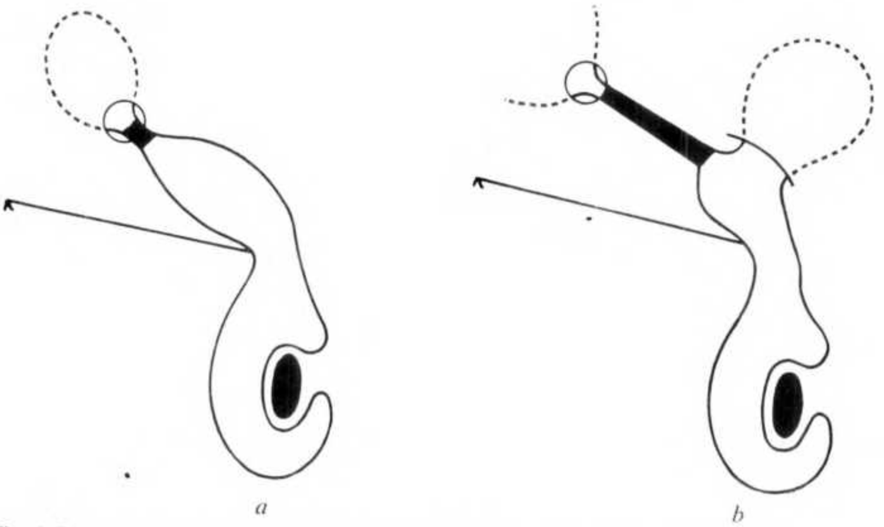


Fig. 4. Diagrams of complete abdominoscrotal hydroceles: *a*, indirect. *b*, direct.

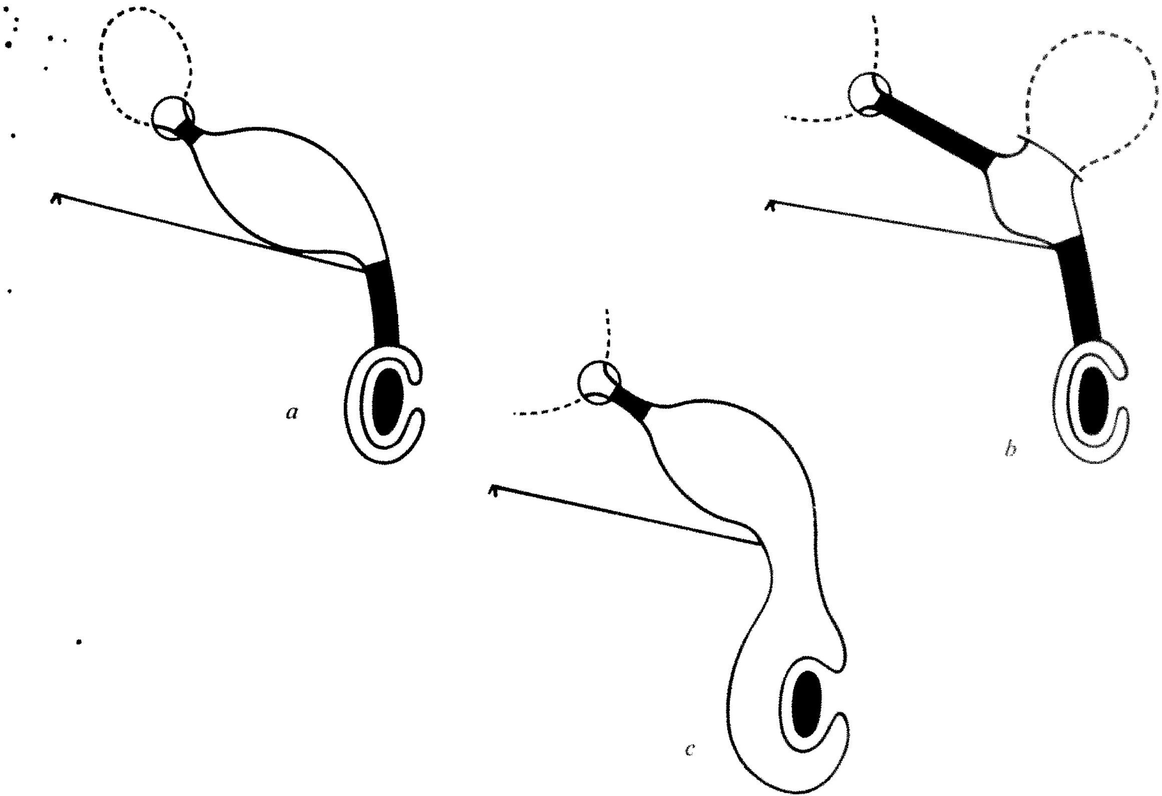


Fig. 5. Diagrams of incomplete abdominoscrotal hydroceles: *a*, indirect abdomino-inguinal; *b*, direct abdomino-inguinal; *c*, inguinoscrotal.

steady traction and blunt finger dissection with a piece of gauze, the whole abdominal part of the hydrocele sac was pulled out. The larger part of the abdominoscrotal sac was excised and the remaining smaller tunica vaginal part everted. The scrotal incision was closed after leaving a rubber drainage tube in the scrotum. The patient developed a small haematoma in the lower abdomen which gradually subsided, and he was discharged from hospital on 17 May, i.e. 19 days after the operation.

Discussion

Incidence

Although since its first description in 1834 only 62 cases of abdominoscrotal hydrocele had been collected from the literature up to 1964, during the past 10 years 21 cases have been reported, all from India. It is probable that many cases have remained unreported in the past.

Aetiology

Dupuytren (1834) suggested that a vaginal hydrocele may, on increasing distension, push its way up through the inguinal canal and assume an abdominal position. Kocher (1878, 1887), Currie (1953) and Burkitt and Williams (1964) shared this view. However, it appears unlikely that a vaginal hydrocele, instead of distending the scrotum, would on enlarging enter the external inguinal opening and then the inguinal canal to find its way into the properitoneal space through the internal inguinal ring. We believe that it would be possible only if an increasing vaginal hydrocele opens up a partially obliterated processus vaginalis from below upwards to a point where the processus vaginalis is firmly obliterated.

It is generally believed that in abdominoscrotal hydrocele the scrotal swelling usually precedes the onset of the abdominal one (Mitra et al., 1972). *Case* 2 in the present report is therefore of special interest. This patient had an abdomino-inguinal hydrocele. It seems that the initial lesion was an encysted type of the hydrocele of the cord situated in the proximal part of the inguinal canal reaching the internal ring. The proximal end, on distending, invaginated the internal ring and formed the properitoneal abdominal part of the hydrocele sac.

We suggest that abdominoscrotal hydroceles should be classified as follows:

1. Complete abdominoscrotal hydrocele (*Fig.* 4).
   - *a.* Indirect type (*Fig.* 4*a*).
   - *b.* Direct type (*Fig.* 4*b*).
2. Incomplete abdominoscrotal hydrocele (*Fig.* 5).
   - *a.* Abdomino-inguinal hydrocele.
     - i. Indirect type (*Fig.* 5*a*).
     - ii. Direct type (*Fig.* 5*b*).
   - *b.* Inguinoscrotal hydrocele (*Fig.* 5*c*).

Excision

It is now generally accepted that excision of the abdominal part of the sac and eversion of the tunica vaginalis is the treatment of choice. Many incisions have been advocated to achieve this. We now believe that a conventional inguinal incision with the technique employed by Lord (1959) in the direct type, and the technique used by us in the indirect type of abdominoscrotal hydrocele will serve the need adequately. Reduction of the size of the hydrocele after exposure, by aspiration or tapping, makes the incision easy, and a postoperative pressure bandage for 48 hours prevents large haematoma formation.

References

BICKLE L. W. (1919) Abdominal or bilocular hydrocele. *Br. Med. J.* **2**, 13.

BURKITT D. and WILLIAMS E. H. (1964) Abdominoscrotal hydrocele. *Br. J. Surg.* **51**, 154–155.

CURRIE J. A. (1953) Cited by LORD (1959) and BURKITT and WILLIAMS (1964).

DUPUYTREN G. (1834) Cited by PRATHER (1942).

HOLMES J. M. (1932) A case of properitoneal hydrocele. *Br. J. Surg.* **20**, 346–348.

JACOBSON W. H. A. (1893) Cited by PRATHER (1942).

KOCHER T. (1878) Cited by PRATHER (1942).

KOCHER T. (1887) Cited by PRATHER (1942).

LISTER J. (1856) Cited by PRATHER (1942).

LORD M. D. (1959) A case of abdomino-scrotal hydrocele. Hydrocèle en bissac. *Br. J. Surg.* **46**, 645–646.

MITRA S. SINGH R. and GOPAL S. (1972) Abdominoscrotal hydrocèle (hydrocèle en bissac) *J. Indian Med. Assoc.* **59**, 392–393.

PRATHER G. C. (1942) Abdominoscrotal hydrocele. Review of the literature and report of a case. *New Engl. J. Med.* **226**, 255–260.

When pseudomonas threatens...

Pyopen

The skill of the surgical team, hours in the theatre, the most advanced techniques in the world . . . and infection can still throw the outcome into jeopardy.

Systemic pseudomonas or proteus infections call for Pyopen. Only Pyopen offers you good activity against these Gram-negative organisms with the added advantage of penicillin safety.

Intravenous Pyopen, at a dosage of 5g 4–6 hourly will rapidly control many of these dangerous infections. And Pyopen is also suitable for long-term therapy and for patients with lowered host defences.

Adult Dosage
5g I.V. 4–6 hourly.
In patients with renal impairment dosage may be reduced; monitoring is advisable in these cases to ensure adequate serum antibiotic levels.
Contra-indication
Penicillin hypersensitivity.
Side-effects
As with other injectable penicillins. In rare cases, skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Pyopen–by infusion or injection

Further information is available on request.
Pyopen* (carbenicillin sodium B.P.) is a British product originated by
Beecham Research Laboratories, Brentford, England. *regd.

NOW
MORPHINE
MINUS
VOMITING

CYCLIMORPH
TRADE MARK

CYCLIMORPH Injection has all the benefits of morphine plus an effective anti-emetic, cyclizine – in a single injection.

Cyclizine significantly reduces the incidence of nausea and vomiting,[1] whether associated with the condition or morphine-induced.

CYCLIMORPH is indicated in all conditions where morphine is needed.

[1] *Br. J. clin. Pharmac*, (1975), 2, 81.
Full prescribing information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd.
Berkhamsted, Herts

Br. J. Surg. Vol. 62 (1975) 633

Triorchidism with normal spermatogenesis: an unusual cause for failure of vasectomy

M. HAKAMI AND S. H. MOSAVY*

SUMMARY

The wife of a vasectomized man became pregnant by her husband. He was examined and a supernumerary testis with intact vas and with normal histology and normal spermatogenesis were discovered.

TRIORCHIDISM is a rare anatomical entity. Wescott and Dykhuizen (1967) adequately described the embryological development of supernumerary testes. Twenty-four cases have been reported previously, and only 5 patients in addition to the one presented here have shown spermatogenesis (Jichlinski and Ward-McQuaid, 1963; Corwin et al., 1970; Smart, 1972).

Case report

The patient, aged 45 years and father of 4 children, was first referred to us because, in spite of bilateral vasectomy 2 months before, his wife had developed amenorrhea of 4 months' duration. Semen analysis had not been performed following vasectomy. On examination the patient appeared normal except that two lumps were detected in the right hemiscrotum which felt like small testes and did not permit transillumination. Both had firm cord-like structures palpable up to the external inguinal ring. The left testis was normal. Laboratory investigations including excretory urography were normal. Semen analysis revealed normal spermatogenesis. On examination his wife was thought to be pregnant, compatible with 4 months' duration of amenorrhea.

A presumptive diagnosis of triorchidism was made, and at operation, under local anaesthesia, two vasa deferentia were detected in the right scrotum and were exposed throughout their length, during which it became evident that one of them had previously been partly resected. A further 1-cm length of the upper end of this vas deferens was excised. The second vas deferens on the same side was seen to be intact and measured 4 cm. At no point did the two structures communicate. A 2-cm length of this supernumerary vas deferens was resected. Both right hemiscrotal testes were biopsied and showed normal histology. In addition, the testis with the intact vas deferens showed normal spermatogenesis (*Fig.* 1). On the left side a partly resected vas deferens was present. A second resection was performed on the upper end. Histological examination of the three resected vasa deferentia established their nature so that triorchidism with normal spermatogenesis was confirmed. The problem was explained to the patient and his wife.

Discussion

The first histologically proved case of polyorchidism was reported by Lane in 1895. Since then sporadic cases have appeared in the literature (Boggon, 1933; Jichlinski and Ward-McQuaid, 1963; Wescott and Dykhuizen, 1967). The condition may be associated with other congenital abnormalities including anomalous union between the testis and its epididymis, fixation of the epididymis to the testicle in its unusual anatomical position, absence of a rete testis and/or absence of all epididymal appendage, hernia and hydrocele (Corwin et al., 1970).

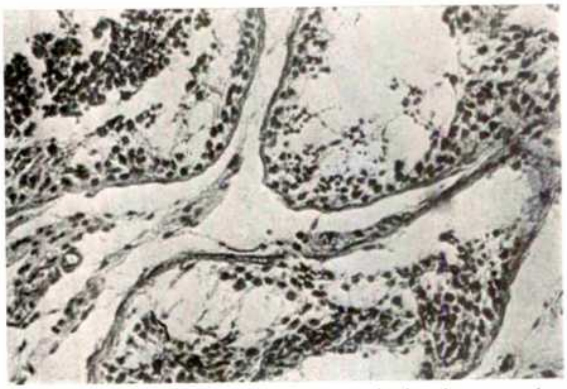


Fig. 1. Section of the supernumerary testis showing normal spermatogenesis.

This report emphasizes the need for a thorough urogenital examination before vasectomy and a further, if unusual, justification for the performance of routine postvasectomy semen analysis.

References

BOGGON R. H. (1933) Polyorchidism. *Br. J. Surg.* **20**, 630–639.

CORWIN S.H., ADDONIZIO J. and NAGAMATSU G. R. (1970) Polyorchism with anomalous urogenital union. *J. Urol.* **104**, 346.

JICHLINSKI D. and WARD-MCQUAID N. (1963) Duplication of the testis and infertility. *J. Urol.* **90**, 583–587.

LANE W. A. (1895) Polyorchidism. *Trans. Clin. Soc. Lond.* **28**, 59.

SMART R. H. (1972) Polyorchism with normal spermatogenesis. *J. Urol.* **107**, 278.

WESCOTT J. W. and DYKHUIZEN R. F. (1967) Polyorchism. *J. Urol.* **98**, 497–500.

---

* Department of Surgery, Isfahan University, School of Medicine, Isfahan, Iran.

Br. J. Surg. Vol. 62 (1975) 634–637

Immediate operative fitting of upper limb prosthesis at the time of amputation

K. P. ROBINSON, B. G. ANDREWS AND M. VITALI*

SUMMARY

Three patients are described—2 with an above-elbow amputation and 1 with a through-wrist amputation—in whom a temporary prosthesis was applied on the operating table and in all of whom function was rapidly established. The patients did not become one-handed, with the result that they have all continued to wear their prosthesis throughout their working hours and use their artificial hand for all everyday functions. The value of this technique in making the patient accept the prosthesis and therefore to make full use of it suggests that this procedure should be more widely applied in patients who require upper limb amputation.

AMPUTATION of the upper limb is less frequently performed than lower limb amputation, but on the occasions when the operation is performed the patient concerned is usually of a younger age group and the loss of part of an upper limb represents a more extreme disability, particularly when the sophisticated function of the human upper limb is considered. Many patients who have an upper limb amputation prefer not to wear an artificial limb and therefore do not obtain any benefit from a prosthesis. One reason for this is that once all or part of an upper limb is amputated the patient quickly learns to compensate the loss by the use of the remaining normal upper extremity, often to such good effect that the apparently cumbersome prosthesis is never accepted and frequently abandoned.

To prevent this rejection of an upper limb prosthesis it is felt that the immediate fitting on the operating table maintains a complete body image and cerebral representation of the missing extremity so that the patient can make the best use of the prosthesis from that time onwards. In addition, the thought that there will be some extremity after the operation which friends and visitors can see, to some extent cushions the mental trauma of the amputation and on occasion, when the operation is performed for malignant disease, may enable the patient to accept the advice for this radical treatment more readily.

Three patients are described in whom upper limb amputation was performed and an upper limb prosthesis fitted immediately which was worn continuously from that time onwards.

Case reports

Case 1: H. M. aged 12 years. One year previously a swelling of the left wrist had been biopsied and a diagnosis of osteosarcoma was made which was treated by radiotherapy with cobalt-60 to a total tumour dose of 6000 R. For 6 months prior to his admission to Queen Mary's Hospital, Roehampton, the left wrist, palm and dorsum of the hand had been swollen and the patient had been unable to supinate or pronate the left forearm. His general health, however, remained completely satisfactory. At that time a hardened swelling was noted around the left wrist, and a soft swelling over the medial part of the palm and over the fourth and fifth metacarpals. An X-ray of the forearm showed that there was less sclerosis in the radial shaft than had previously been seen and the appearances were those of osteogenic sarcoma modified by radiotherapy. A chest X-ray showed no abnormality.

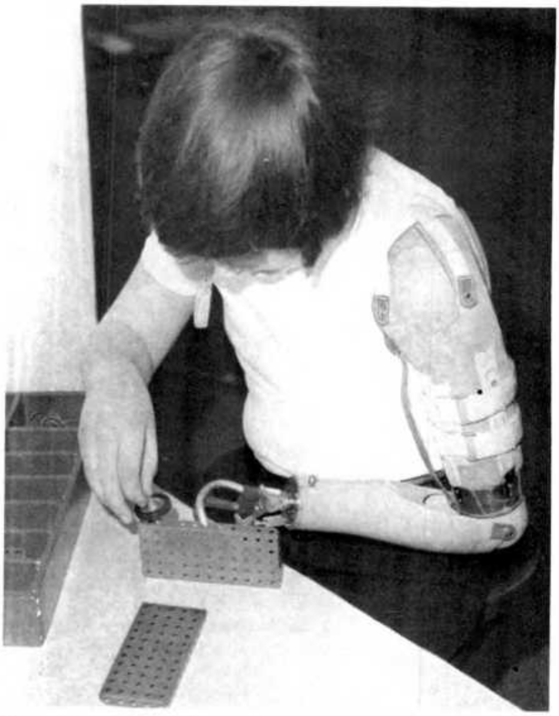


Fig. 1. *Case* 1. Learning to use the split hook on the third postoperative day.

On 6 February 1973 a left above-elbow amputation was performed (K. P. R.) under a general anaesthetic, using equal flaps and a level of bone section 10 cm above the medial epicondyle. The end of the humerus was filed to a rounded outline and the flexor and extensor muscle groups were sutured over the bone end to constitute a full myoplasty. All the major nerves were sectioned above the level of amputation and all vessels were ligated. The skin was closed with interrupted fine nylon sutures and no drainage was provided. The stump was bandaged with a thin crêpe bandage and the above-elbow prosthesis was applied on the operating table. After operation the prosthesis was removed for inspection of the wound on the second postoperative day and replaced without difficulty. The patient made increasing use of the prosthesis, wearing the

---

* Queen Mary's Hospital, Roehampton, Westminster Hospital Group, London.

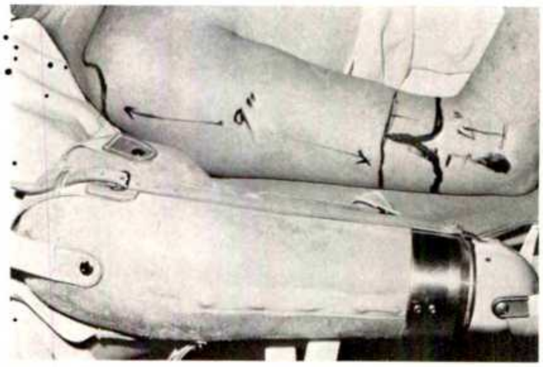


Fig. 2. *Case* 2. Skin incision marked before operation. All the measurements were checked with the prosthesis which had been supplied the previous day.

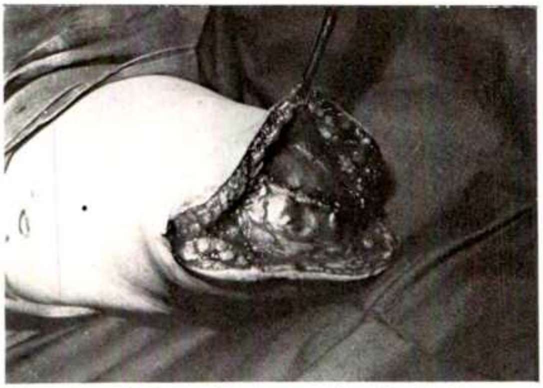


Fig. 3. *Case* 2. Above-elbow amputation showing the myoplastic attachment of flexor and extensor muscles over the bone end.

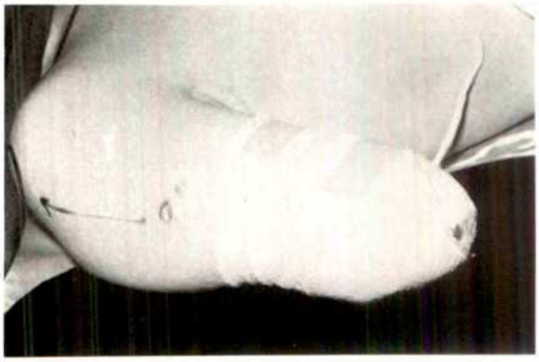


Fig. 4. *Case* 2. Completed stump covered by single crêpe bandage.

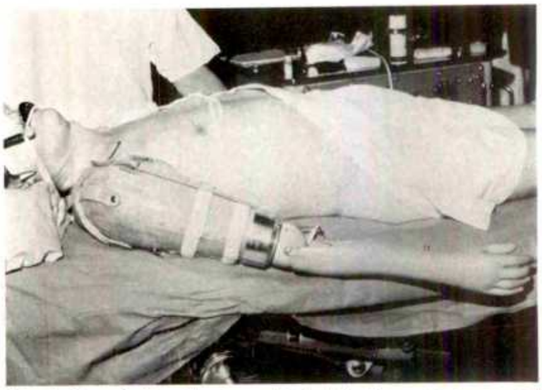


Fig. 5. *Case* 2. Prosthesis applied while the patient was still anaesthetized. A Plastazote shell covered the bandage, under the prosthesis.

cosmetic hand at all times except when he was using the split hook for everyday tasks. The wound healed without difficulty, and within 3 days of the operation the patient was using the prosthesis competently under instruction in the Arm Training School (*Fig.* 1). By the time of his discharge, 4 weeks after his operation, he was using the arm without difficulty and was able to return to school, where he has continued with his education, and he takes part in normal school activities.

One year after operation an opacity appeared in the left chest. Subsequent thoracotomy showed this to be a metastasis and the patient is currently completing a further course of radiotherapy to the chest. He has been supplied with a new prosthesis which he is using continuously for all normal activities.

Histological examination of the metastasis from the lung showed the appearances of a chondroblastic osteogenic sarcoma similar to those of the tumour in the resected forearm.

Case 2: D. B. aged 44 years. In 1955 this patient developed osteoclastoma of the right radius which was treated by curettage followed by radiotherapy to a dose of 3200 R which left the patient with good function and mobility. However, in the year prior to admission he developed increasing discomfort and pain with any undue use of the wrist. X-rays taken at that time showed increased bone destruction, but his chest X-ray remained clear. Biopsy taken then showed the changes of fibrosarcoma, and an isotope bone scan showed an area of increased uptake of strontium at the lower end of the right radius. Whole lung tomography failed to demonstrate any metastasis. Amputation was advised at a level which would clear the radius and ulna and the patient was transferred to Queen Mary's Hospital, Roehampton, where a prosthesis was constructed for an above-elbow amputation. The patient was introduced to the Arm Training School and the appliances which he would use with his prosthesis.

Operation (*Fig.* 2) was performed on 5 February 1974 (K. P. R.) Bone section was 22 cm from the acromion process and at this level equal flaps were cut. All the nerves were cut proximal to the line of bone section and the muscles distal to the line of section to enable a myoplastic closure across the bone end (*Fig.* 3). The bone end was carefully rounded with a bone file and all the muscle groups secured over it with catgut sutures. The deep fascia was sutured and the skin closed with interrupted nylon without any drainage. A small crêpe bandage was applied (*Fig.* 4) and covered by a Plastazote cuff and the prosthesis (*Fig.* 5). Three days later the patient was beginning to use his prosthesis and the wound healed without difficulty, the sutures being removed on the fourteenth day. The prosthesis was subsequently modified so that the Plastazote cuff was unnecessary, and the patient continued his arm training on an outpatient basis. He has become left-handed for the purposes of writing but is already able to drive his car and to manage tools such as a knife and fork with his split hook (*Fig.* 6). He wears the arm continuously during his waking hours and has continued to do so up to the present time, 11 months later.

Histology of the forearm showed a moderately well-differentiated fibrosarcoma with conspicuous mitotic activity. The appearance is that of a fibrosarcoma in an area of radiation for a previous osteoclastoma.

Case 3: V. W. aged 54 years. This patient was admitted in May 1971 with a history that a year previously he had sustained a chain-saw injury to his left wrist, dividing all flexor tendons except the flexor pollicis longus and all the extensor tendons together with both median and ulna nerves. The distal row of carpal bones at the bases of the metacarpals were also extensively damaged. The possibility of reconstructive surgery was extensively considered but eventually the patient accepted

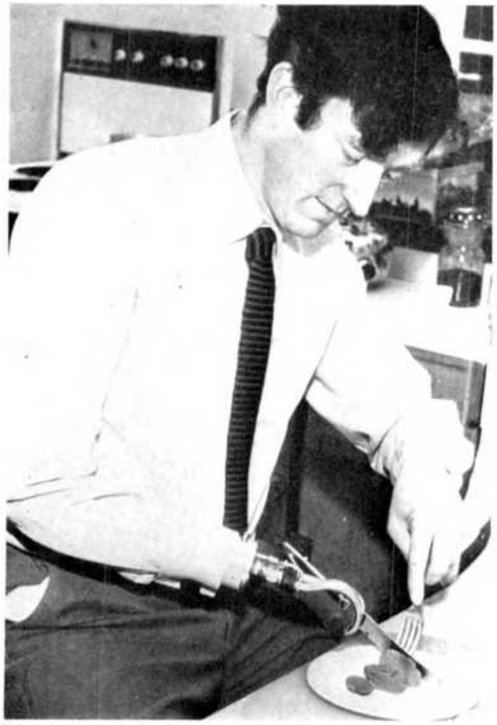


Fig. 6. *Case* 2. Using a knife and fork 2 weeks after operation.

that an amputation and prosthesis would give him the best functional result. The patient was self-employed as a chartered accountant and he was right-handed.

Operation was performed in May 1971 (B. G. A.) when anterior and posterior flaps were formed at wrist level and all tendons, vessels and nerves were divided. The radial styloid was removed and the flexor and extensor tendons were sutured over the bone ends. The wound was closed in layers with a Redivac drain. A soft gauze dressing was applied, covered with a bandage and a plaster socket constructed over this carrying a double hook (*Fig.* 7). A shoulder harness was attached. The wound healed without difficulty, and within 48 hours the patient was able to use his prosthesis (*Fig.* 8), and at the end of 18 days he had become efficient with the split hook which he used for all his everyday activities.

Six weeks after operation he received his definitive prosthesis together with a cosmetic hand. When reviewed 18 months after operation it was noted that he had made a great success of wearing the prosthesis and was using it for gardening, carpentry and driving his car. He was aware of a phantom limb but this caused him no distress.

Discussion

The technique of amputation was standard without involving any modification of the ordinary surgical procedure. The application of a hard shell to the wound dressing was shown to have no deleterious effect on wound healing. The ability of the patient to wear and use a prosthesis from the moment of operation has undoubted advantages.

The concept of immediate fitting of a prosthesis at operation is not new. Berlemont pioneered this technique with the lower limb in 1961 (Berlemont, 1964), soon followed by Dederich (1967) and Burgess et al. (1969), who have treated a large number of patients in this way. However, our own experience with immediate prosthesis fitting after lower limb amputation has confirmed the beneficial effect of immediate fitting and some of the advantages of a rigid socket bearing a prosthesis. We have, however, become aware of problems with pressure necrosis of skin flaps and the problems of infection under the rigid socket in the lower limb, but this has been in patients with arteriosclerotic disease of the lower limb in whom the vascular supply for the skin flaps has been critical, a situation which is not encountered with the upper limb where the amputation is usually performed for disease other than arterial insufficiency and the patients are not so old. Also, in the arm there is little chance of the wound becoming contaminated with *Clostridium* spores, so the risk of anaerobic infection is much reduced. Therefore the use of an immediate prosthesis appears to carry very little risk to the primary healing of the patient's stump.

The number of patients who can be seen in everyday life who are not wearing an upper limb prosthesis is evidence of the speed at which patients become one-handed, even when the dominant hand is lost. Once this has occurred, the most enthusiastic patient is unlikely to persevere to make an upper limb prosthesis work for him in his daily life. We therefore

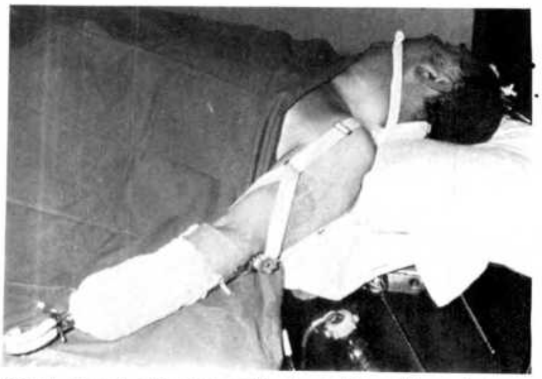


Fig. 7. *Case* 3. Through-wrist amputation with a plaster socket and harness applied while the patient was still anaesthetized. Suction drain tube and split hook can be seen.

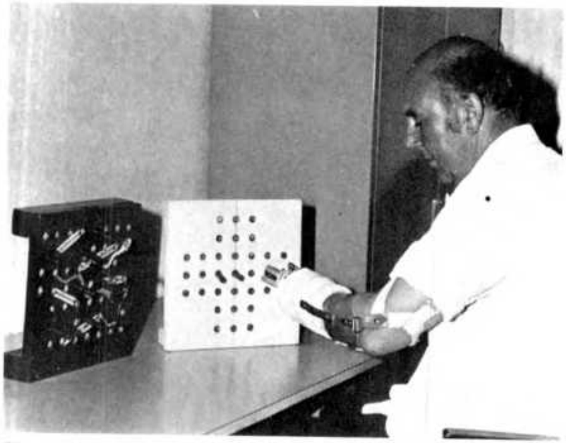


Fig. 8. *Case* 3. Learning to use the split hook on the third postoperative day.

consider it of great importance that the patient is never allowed to become one-handed in his cerebral representation and his mental processes. The instantaneous replacement of the amputated limb with a prosthesis appears to be the most rational way of achieving this end.

All the reported cases attended the Arm Training School within 2 or 3 days of their operation and were already learning to use a split hook before the sutures were removed, with the result that a knife and fork or simple tools could be used at the time that the patient was discharged from hospital. All the patients were wearing their arm throughout their waking hours when they were discharged from hospital and have continued to do so since. The patients who had an above-elbow amputation have had a formal prosthesis made prior to the amputation, while in the third patient a plaster socket was formed on the operation table on top of a soft surgical dressing, and the split hook and attachment were incorporated in the plaster so that the whole could be retained with a harness and shoulder band. Thus, the split hook could operate from the time that the patient regained consciousness. There was no problem in removing and replacing the socket until the time that the definitive prosthesis was constructed.

This follows the method used by Seddon (1966), when a plaster socket and prosthesis were applied at the time of an above-elbow amputation which was combined with a shoulder arthrodesis. Sarmiento et al. (1969) reported a further 4 cases. Loughlin (1969) used the technique in a bilateral arm amputation. Tooms (1972) discussed the advantages of the method and clinic reports of its use in the treatment of a large number of patients. He drew attention to the value of suction drainage and referred to the problem of distal oedema which may result if proximal constriction is inadvertently applied by the dressing, bandage or socket. He suggested that a plaster socket is most suitable for below-elbow amputations while a conventional prosthesis can be used for amputations at above-elbow level.

Conclusions

There appears to be no surgical disadvantage in applying a prosthesis to an upper limb amputation on the operating table and the benefit to the patient is unquestionable. For amputation below the elbow a plaster socket is the most satisfactory, but above this level a prosthesis can be made prior to the operation and applied over the surgical dressing.

Acknowledgements

We would like to thank the surgeons who referred these patients to the Westminster Hospital Group for their permission to publish these cases, the Department of Health and Social Security for allowing access to the Limb Fitting Service files, the Photographic Department at Queen Mary's Hospital, Roehampton, for the illustrations and Miss R. Clark for typing the manuscript.

References

BERLEMONT M. (1964) Paper given at the International Conference of Physical Medicine, Paris.

BURGESS E. M., ROMANO R. L. and ZETTL J. H. (1969) *The Management of Lower Extremity Amputations*, TR 10–6. Prosthetic and Sensory Aids Service. Washington, DC, Veterans Administration, p. 11.

DEDERICH R. (1967) *Symposium on Immediate Post-operative Fitting. Ministry of Health. Biochemical, Research and Development Unit Report.*

LOUGHLIN E. (1969) Immediate postsurgical prosthesis fitting of a bilateral below-elbow amputation—a report. *Prosth. Int.* 3, 47–49.

SARMIENTO A., MCCOLLOUGH N. C., WILLIAMS E. M. and SINCLAIR W. F. (1969) Immediate post-surgical prosthetics fitting in the management of upper extremity amputations. Artificial limbs. *Prosth. Int.* 3, 45–47.

SEDDON SIR HERBERT (1966) Personal communication. Above-elbow amputation with arthrodesis of shoulder.

TOOMS R. E. (1972) Amputation surgery in upper extremity. *Orthop. Clin. North Am.* 3, 383–395.

Br. J. Surg. Vol. 62 (1975) 638–641

The bacteraemia associated with burns surgery

C. H. BEARD, C. D. RIBEIRO AND D. M. JONES*

SUMMARY

Fifty-four surgical procedures on 39 burnt patients were studied with serial blood cultures. In 25 (46 per cent) of these procedures the cultures were positive. In spite of the absence of prophylactic systemic antibiotics there were no clinical manifestations and not one of the bacteraemias developed into a septicaemia.

The role of natural immunity in controlling the bacteraemia is discussed and it is suggested that prophylactic systemic antibiotic therapy covering burns surgery is unnecessary in the presence of normal immunoglobulin levels.

BACTERAEMIA frequently accompanies the manipulation of infected tissues. This phenomenon has been well documented in relation to procedures in dentistry (Felix et al., 1971), otorhinolaryngology (Herzen, 1971), surgery on the large bowel (LeFrock et al., 1973) and operations on the genito-urinary tract (Sullivan et al., 1973). We have investigated the possibility of bacteraemia occurring when the burn wound in patients is manipulated during surgical procedures.

Patients

Fifty-four unselected procedures under general anaesthesia on 39 burnt patients were studied by serial blood cultures. All the patients were inpatients at the Manchester Regional Burns Unit at Withington Hospital. The treatment policy at the time of this study consisted of closed dressings followed by varying degrees of active slough removal, from shaving excision with a grafting knife to blunt dissection with or without immediate grafting. These procedures were carried out between the tenth and fiftieth days after burning. During the period of the study no systemic antibiotics were used routinely and neither topical silver nitrate nor Sulfamylon nor silver sulphadiazine were used. In order to establish the immune status the immunoglobulin levels were measured in some patients.

The patients studied had deep burns extending to up to 60 per cent (average 15 per cent) of the body surface and were between the ages of 14 and 86 years (average age 45·5 years).

Methods

During this investigation burns were swabbed routinely once each week. The organisms isolated were characterized by standard methods and these results were used to establish whether organisms grown from blood cultures were also present on the burn wounds.

Blood cultures

Blood samples were taken only from veins selected to be away from the burned areas so that the possibility of skin contamination by colonizing bacteria was minimized. Most commonly veins in the back of the hand were used. The skin was prepared by swabbing with 70 per cent isopropyl alcohol and allowing this to dry before venepuncture. Ten ml of blood were collected immediately preoperatively and then intermittently during the procedure, but usually after 5 minutes and then at 15-minute intervals until the end of the procedure.

Castaneda broth culture

Two ml of blood were added to a bottle containing a slope of 15 ml of blood agar base no. 2 stiffened by the addition of 0·5 per cent Ionagar no. 2 (Oxoid L12) and covered by 70 ml of brain heart infusion broth containing 0·03 per cent Liquoid (sodium polyanethol-sulphonate).

Pour plate

One ml of blood was added to 9 ml of brain heart infusion broth (Oxoid CM225) containing 0·5 per cent white saponin and 0·5 per cent trisodium citrate. This was then added to 10 ml of molten-cooled double strength blood agar base no. 2 (Oxoid CM271) poured into a plastic Petri dish and allowed to set.

Filtration

The remaining 7 ml of blood were added to 100 ml of 0·05 per cent aqueous Triton 100 containing 0·5 per cent sodium carbonate. This was transferred, using a sterile syringe and needle, to a Sterifil filter system (Millipore) containing 45-mm membrane as soon as possible after being taken. After filtration by suction the membrane was washed with a total of 60 ml of nutrient broth. The filter carrier was then opened in a bacteriological cabinet and the membrane was transferred aseptically to the surface of a blood agar plate.

All the cultures were incubated aerobically at 37 °C. The pour plate and the membrane were inspected at 18 hours and again on the second day and discarded if there was no growth. The broth culture bottles were examined daily for growth for 7 days and if no growth was visible they were subcultured on the seventh day.

Immunoglobulin estimation

IgG and IgM levels were measured by a radial diffusion method using Hyland Immuno-Plate plastic

---

* Departments of Plastic Surgery and Bacteriology, Withington Hospital, Manchester.

Table I: NUMBER OF PROCEDURES PRODUCING EACH BACTERIAL SPECIES

Organism:	No. of cases:
Staphylococcus aureus	12
Pseudomonas aeruginosa	9
Proteus mirabilis	8
Enterococci	3
Providence sp.	1
Proteus morgani	1
Bacteroides sp.	1
Candida albicans	1
Aerobacter aerogenes	1
Escherichia coli	1

Table II. NUMBER OF ORGANISMS PER ML OF BLOOD IN 13 SAMPLES

Organism:	No./ml blood:
Staph. aureus	0·14
Staph. aureus	1·0
Enterococcus sp.	0·6
Enterococcus sp.	0·9
Enterococcus sp.	0·14
Staph. aureus	0·14
Staph. aureus	0·4
Ps. aeruginosa	0·14
Ps. aeruginosa	16·0
Enterococcus sp.	0·14
Staph. aureus	0·3
Staph. aureus	0·14
C. albicans	0·14

slides. The results were calculated from a graph using the results of known standards. The limits of normality accepted were those proposed by Hobbs (1970).

Results

Bacteraemia was detected during 25 out of 54 procedures; no growth was obtained in any of the 50 preoperative cultures. Bacteria were grown from 38 out of 111 (34 per cent) cultures taken at operation. A single bacterial species was grown in 13 operations, 2 in 11 and 3 in 1. *Table I* shows the frequency with which various organisms were isolated. All the organisms were present on the burn wound or had been isolated shortly before the operation.

On 13 of the samples quantitative cultures were performed; the numbers of organisms ranged from 1 in 7 ml of blood to 16 organisms per ml, the average being 1 organism to 3 ml of blood (*Table II*).

When an organism was grown on more than one occasion during a procedure the positive cultures were usually close together (*Fig.* 1).

The clinical course of patients who had had a positive blood culture was compared with those who had not. The mean twice daily temperatures for 48 hours before and after the day of operation were compared and the greatest difference in the mean temperatures was not found to be significant (P = 0·25) (*Fig.* 2). Shock, hypotension or rigors were not seen. *Figs.* 3 and 4 show the distribution of the ages and the size of the original burn in the two groups; it must be stressed that the total raw area at the time of the operation was sometimes small.

The nature of the operations was compared in the two groups. Twenty-one of the operations lasted for more than 1 hour and of those, 13 (62 per cent) developed a bacteraemia, while only 12 of the 32 shorter operations did (37 per cent). Breach of the granulation tissue barrier was also recorded. This barrier was

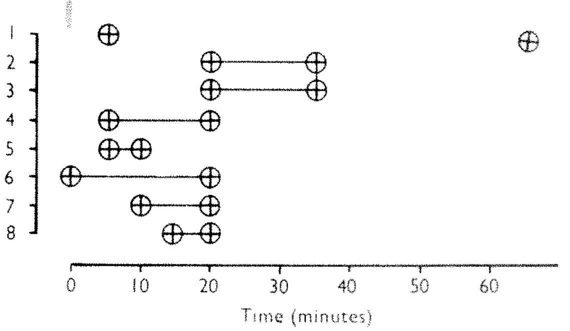


Fig. 1. The timing of positive blood cultures when the same organism was isolated on more than one occasion during a procedure.

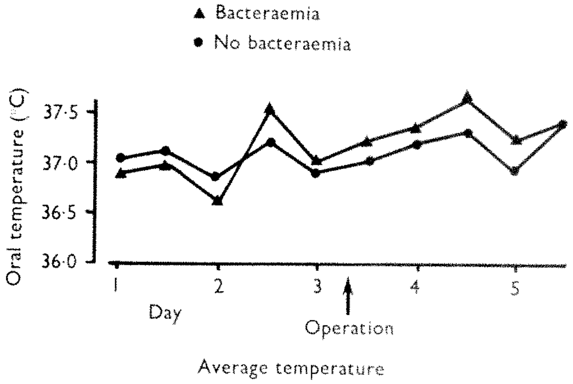


Fig. 2. Mean twice daily temperatures of patients with and without bacteraemia.

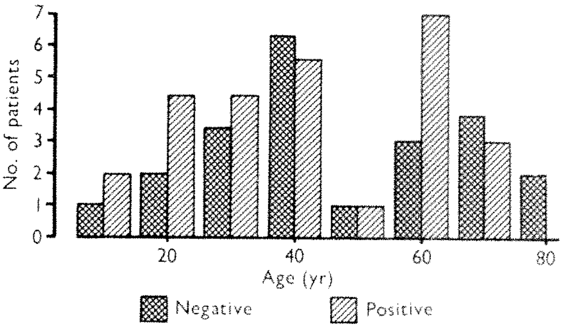


Fig. 3. Age of patients with and without bacteraemia.

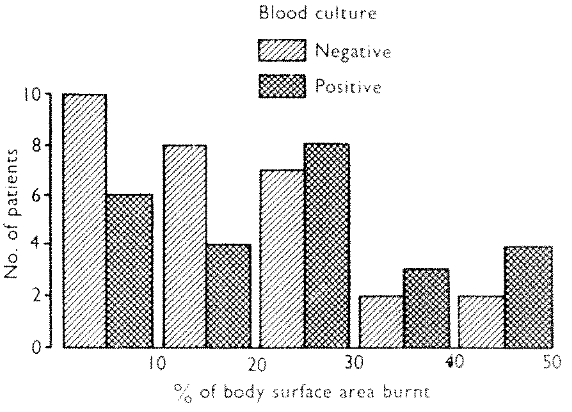


Fig. 4. Original burn size related to presence or absence of bacteraemia.

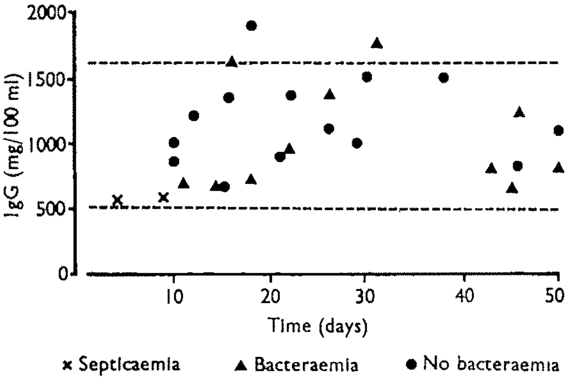


Fig. 5. IgG levels at time of operation.

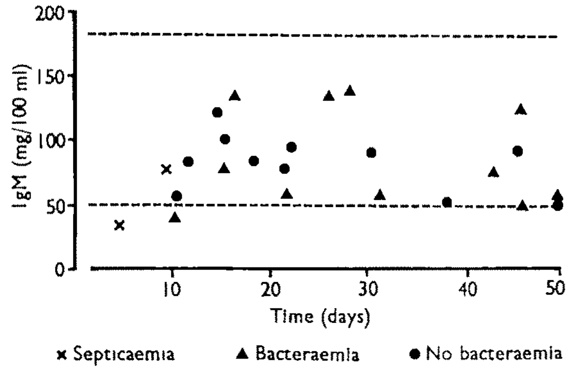


Fig. 6. IgM levels at time of operation.

considered broken when the burn was excised, opening up tissue planes. This happened in 12 of 26 (46 per cent) procedures, producing bacteraemia, while its preservation by conservative slough removal liberated detectable bacteria in 13 out of 27 cases (48 per cent).

In *Figs.* 5 and 6 the IgG and IgM levels are plotted against the day of operation, with the range of normal levels indicated. Included in these figures are the immunoglobulin levels at the time of operation of 2 patients not in the series who subsequently developed septicaemia shortly after surgical procedures on their burns.

Discussion

The study has shown that bacteraemia is a frequent occurrence in burns surgery and that the organisms, being present on the wound at the time of operation or shortly before, are likely to have originated from the burn wound. It is suggested that the bacteraemia was not the chance detection of a few randomly liberated organisms, as in 9 out of 25 operations accompanied by bacteraemia the same organisms were grown on two or more different occasions during the procedure; they are more likely to have been liberated over a period of time during the operation. An attempt was made to establish how various factors influenced the occurrence of bacteraemia. We have no direct evidence of the degree of wound infection other than the presence of the organisms on the burn, but we were unable to detect any significant difference between the mean temperatures of the groups of patients from whom positive or negative blood cultures were obtained during the operation for the 48 hours before the procedure. There was an association between increase in age of the patient and the development of a bacteraemia. The area of the original burn also influenced the occurrence of bacteraemia, though at the time of the operation the raw area was often small. There was a tendency for longer operations to be associated with a bacteraemia, although this was not significant ($P = 0{\cdot}14$). The technique used in the operation was less important; the preservation of an intact 'granulation tissue barrier' did not prevent a bacteraemia developing, nor did its violation by shaving excision (Janzekovic, 1970) or radical excision down to the deep fascia regularly produce bacteraemia.

The immune status of some of the patients was assessed by measuring the serum IgG and IgM levels at the time of operation. These were all found to be normal, probably because the operations were all performed relatively late (after the tenth day) so that the depression (Munster et al., 1966) associated with burning had passed.

The major finding of this study relates to the effects of the bacteraemia. None of our patients was treated with prophylactic systemic antibiotics and yet the organisms disappear spontaneously from the circulation. More significant was the complete absence o clinical manifestations; in many studies on the bacteraemia produced by manipulations of infected tissues, shock, hypotension and rigors have been reported. Sullivan et al. (1973) reported that half o the transurethral prostatectomies that were associated with positive blood cultures produced these symptoms Our patients, in contrast, did not have these symptoms despite the fact that we recovered approximately similar numbers of organisms from the bloodstream Further, we were unable to demonstrate any significant difference in the mean temperatures of the two groups in the first 48 hours after operation.

Thus, the patients have dealt with the challenge o the bacteraemia unaided, presumably by the natural immune defences against the organisms concerned Two patients not in the series who had developed septicaemia shortly after a surgical procedure wer studied retrospectively. These operations had bee performed relatively early after burning and as can b seen from *Figs.* 6 and 7 where the IgG and IgM level have been plotted against the time of operation bot of these were low or at the lower limit of norma We interpret these findings as reinforcing the view that the normality of the immune status was importan in protecting our patients in this series from the effec of the bacteraemia.

It is suggested that routine systemic antibioti therapy has no part in preventing the establishmen of systemic bacterial infection when patients ar operated upon later than 10 days after sustaining th burn.

Acknowledgements

We are grateful to the consultant plastic surgeons at Withington Hospital for permission to study the patients under their care.

References

FELIX J. E., ROSEN S. and APP G. R. (1971) Detection of bacteraemia after the use of an oral irrigation device in subjects with periodontitis. *J. Peridontol.* **42**, 785–787.

HERZEN F. S. (1971) Bacteraemia and local infection with nasal packing. *Arch. Otolaryngol.* **94**, 317–320.

HOBBS J. R. (1970) Simplified radial immunodiffusion, Broadsheet No. 68, Association of Clinical Pathologists.

JANZEKOVIC Z. (1970) A new concept in the excision and immediate grafting of burns. *J. Trauma* **10**, 1103–1108.

LEFROCK J. L., ELLIS C. A., TURCHIK J. B. and WEINSTEIN L. (1973) Transient bacteraemia associated with sigmoidoscopy. *New Engl. J. Med.* **289**, 467–469.

MUNSTER A. M., HOAGLAND H. C. and PRUITT B. A. jun. (1970) The effect of traumal injury on serum immunoglobulins. *Ann. Surg.* **172**, 965–969.

SULLIVAN N. M., SUTTER V. L., MIMS M. M., MARSH V. H. and FINEGOLD S. M. (1973) Clinical aspects of bacteraemia after manipulation of the genito-urinary tract. *J. Infect. Dis.* **127**, 49–54.

From an address given by Sir William Thomson at the Opening of the Physical and Chemical Laboratories in University College, Bangor, North Wales, on 2 February 1885.

THERE is this which is satisfactory about it [laboratory investigation] that perseverance is sure to be rewarded. There is no failure in physical science. We do not always find the particular thing looked for; we often find that what we looked for does not exist, or that something else exists very different from what we expected to find; but that something is to be found in any investigation entered upon with intelligence and pursued with perseverance is a certainty.... Every additional knowledge of the properties of matter is of value.

SIR WILLIAM THOMSON (LORD KELVIN) (1894) *Popular Lectures and Addresses*, Vol. 2: *Geology and General Physics*. London, Macmillan, p. 490.

Br. J. Surg. Vol. 62 (1975) 642–644

A rabbit model of perforated appendicitis with peritonitis

D. W. KING, J. F. GURRY, R. B. ELLIS-PEGLER AND B. N. BROOKE*

SUMMARY

No satisfactory animal model simulating acute perforating appendicitis followed by peritonitis in man has hitherto been achieved. A technique has been developed in New Zealand White rabbits to fulfil these desiderata. The bacterial flora associated with the ensuing peritonitis is similar to that found in man both as regards aerobes and anaerobes and their concentrations. The method effectively produces the required model in 70 per cent of rabbits subjected to the experiment. Satisfactory postoperative survival is achieved enabling therapeutic studies.

PRODUCTION of peritonitis experimentally, similar to that in humans, has always been difficult. We have attempted to produce an animal model of peritonitis akin to the human situation.

Materials and methods

Thirty-two New Zealand White rabbits weighing approximately 3000 g were anaesthetized using pentobarbitone induction and maintained by gaseous agents (Hynd, 1975).

Through a lower midline incision the base of the appendix was tied with black silk thread, leaving the blood supply intact (*Fig*. 1). Using the same anaesthetic technique and the same incision, further laparotomy was performed 18 hours after the first operation. If perforation had not occurred spontaneously the appendix was incised near the base, allowing the contents to enter the peritoneal cavity. The wound was then closed. Six hours later, using a gaseous anaesthetic only, appendicectomy was performed through the same incision.

The rabbits were weighed immediately before operation and at the same time each subsequent day.

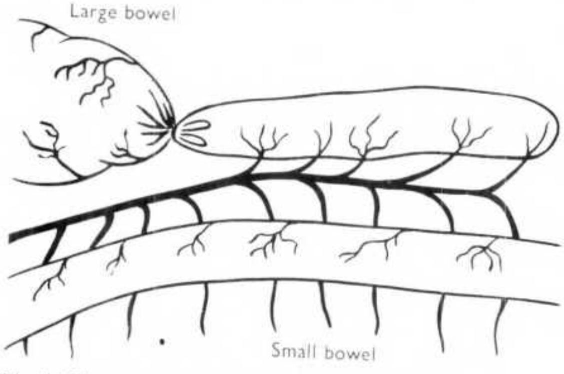


Fig. 1. Diagram showing the method of producing appendicitis.

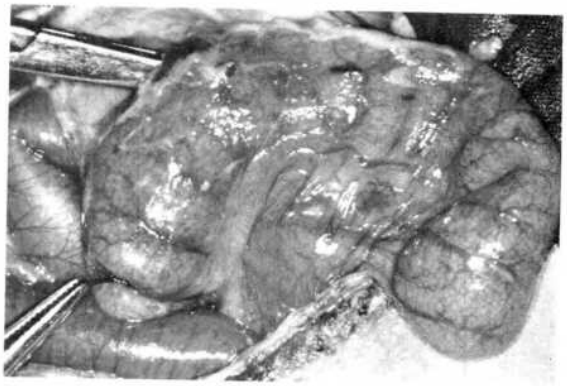


Fig. 2. Appearance of an appendix at the second operation. The upper pair of forceps is inserted through the perforation and the lower pair is holding the base tie.

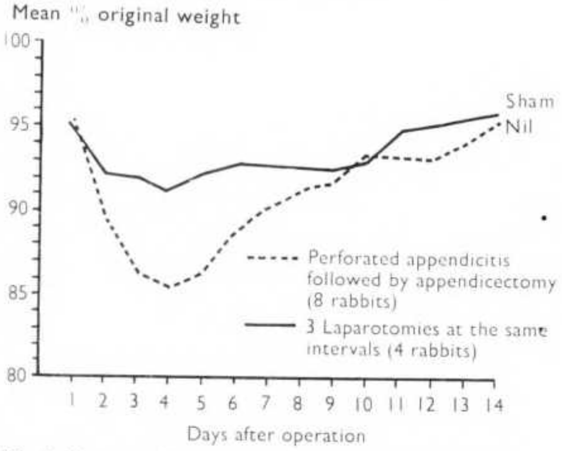


Fig. 3. Postoperative weight changes of the experimental animals compared with those of the controls.

Results

Twenty-eight of the 32 rabbits (87·5 per cent) survived the series of operations and for 36 hours postoperatively; 71 per cent (20 out of 28) of the appendices in the surviving rabbits had perforated spontaneously by the time of the second operation (*Fig*. 2). Of the 28 surviving rabbits, 19 were used in a study which is the subject of another report; 89 per cent (8 out of 9) of the remaining surviving rabbits lived for at least 14 days and were killed during the third week. Post-mortem examination showed a diffuse purulent peritonitis with many adhesions resulting in multiple abscesses throughout the peritoneal cavity, particularly

---

* Department of Surgery and Communicable Disease Unit, St George's Hospital, London.

Present address of D. W. King: St Mark's Hospital, London.

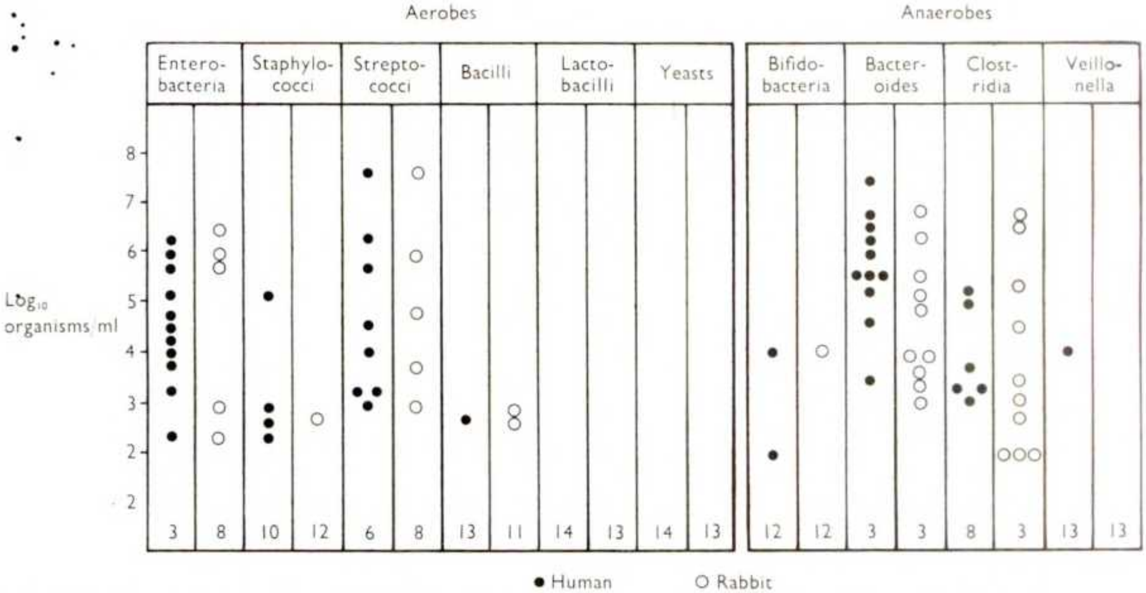


Fig. 4. Comparison of the organisms isolated from 13 rabbits with perforated appendicitis with those in pus found in 14 patients at operation for perforated appendicitis. The number at the base of each column is the number of specimens with a concentration of less than 100 organisms/ml.

the caudal half. Post-mortem examination of the rabbit dying on the third postoperative day showed purulent peritonitis.

Three rabbits in which only a base tie of the appendix was performed had died by 30 hours postoperatively. Tying less of the appendix produced less predictable results; if insufficient was tied, only a localized abscess, without mortality, resulted.

Four control rabbits had laparotomies performed at the same intervals, and at each operation the appendix was brought out on to the abdominal wall for a short time and then replaced. All 4 survived for at least 14 days and lost less weight than the rabbits with peritonitis (*Fig.* 3); no abnormality was found when they were sacrificed. The rabbits with perforated appendicitis followed by appendicectomy lost weight for 4–5 days, then regained weight to reach preoperative levels in the third postoperative week (*Fig.* 3).

Bacteriology

In 13 rabbits, 9 with spontaneous perforations and 4 with artificial perforations, culture of peritoneal fluid present at the third laparotomy was begun within 5 minutes of removal of the sample from the peritoneal cavity. Since the bacterial groups expected in the human situation include enterobacteria, staphylococci, streptococci, bacilli, lactobacilli, yeasts, bacteroides, bifidobacteria, clostridia and veillonella, these organisms were sought in the samples. The viable counts of the bacteria were expressed as $\log_{10}$ organisms/ml of peritoneal fluid; the lower limit of detection of bacteria with this method was 10^2 organisms/ml of fluid (Ellis-Pegler et al., 1975).

A comparison has been made of cultures from 13 animals with those in pus taken at operation for perforated appendicitis with purulent peritonitis in 14 patients (Pickersgill and Ellis-Pegler, 1975) (*Fig.* 4). The distribution was found to be similar; veillonella is an organism not found in the rabbit gut and was only grown from 1 human case.

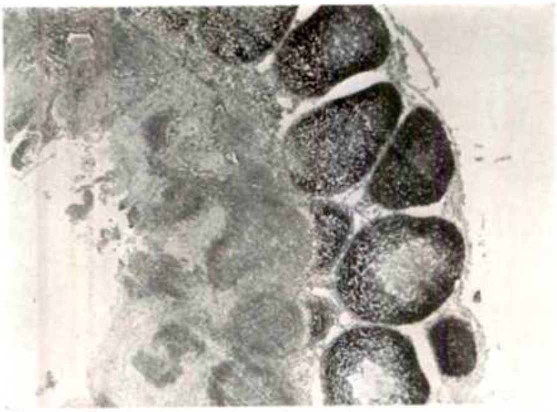


Fig. 5. Histological section of a rabbit appendix showing features similar to those of acute appendicitis in man.

Histology

Histologically, the appearances were similar in all the specimens examined and had many features in common with those seen in acute appendicitis in man (*Fig.* 5). However, in the rabbit suppuration was generally less pronounced and less evenly distributed throughout the wall and there was a zone of suppurative necrosis extending from the mucosa into the superficial parts of the lymphoid follicles. The latter is not seen normally in the human where the process seems to start from a focus rather than diffusely. There was also more lymphoid tissue in the rabbit appendices.

Discussion

Induction of peritonitis in animals by intraperitoneal injection of bacterial suspension alone has proved to be difficult (Browne and Stoller, 1970). Furthermore, rats and mice are relatively resistant to induction of Gram-negative peritonitis (Burnett et al., 1957; Browne and Stoller, 1970). In 1964 Schumer et al. used an injection of a known amount of *Escherichia coli* into the peritoneal cavity of guinea-pigs. Artz et al. in 1962 used pooled filtered faecal suspension, producing at least an 80 per cent mortality rate at 24 hours in dogs; variations on this method have been used often Filler and Sleeman, 1967; Lavigne et al., 1974). Burnett et al. (1957) removed a 3-mm ellipse from the colon of guinea-pigs and found that this routinely produced a severe diffuse peritonitis with an 85 per cent mortality rate. Zintel et al. (1950) induced peritonitis by ligating the appendiceal vessels and the base of the appendix and contaminating the peritoneal cavity with the appendix opened longitudinally; the abdomen was then closed. In 1938 Bower et al. described the technique of isolating and then tying the base of the caecal pouch of dogs, allowing the appendix to perforate spontaneously to produce a spreading peritonitis which in a later series produced a mortality of 78 per cent in untreated animals (Crook et al., 1968). The method was modified by Silvani et al. (1947) to include crushing of the wall of the appendix.

The methods used in injection of known bacterial suspension or perforating the bowel release organisms suddenly into a normal peritoneal cavity, and do not simulate the situation of acute obstructive appendicitis with perforation in humans. The method of Bower et al. (1938) and its subsequent variation (Silvani et al., 1947) involve the production of gangrene of the appendix by tying the blood vessels and do not include removal of the appendix. Neither of these reflect the human situation.

To overcome these objections a model has been created akin to the disease process in man. It is recognized that the faecal and colonic flora of rabbits and man are not identical. Nevertheless, with isolation and identification techniques widely used in human studies the same bacterial groups have been isolated from rabbit and human faeces, although in different concentrations and with some exceptions (Williams-Smith, 1965; Hawksworth et al., 1971). Perforation of the appendix is followed by peritonitis similar in bacteriological flora and degree of contamination to the situation found in humans. Moreover, the immediate effect in the animal is not so overwhelming as to produce rapid death, and this permits assessment of the postoperative course; the degree of peritonitis appears to be reflected in weight loss. Since perforation of the appendix is achieved in 70 per cent of animals the rate of reproducibility of the model is acceptable. If a high mortality is required for study, ligation of the appendix alone without subsequent removal may be undertaken; in this circumstance therapeutic measures under trial should be instituted after 24 hours.

Acknowledgements

We would like to thank Dr J. P. O'Sullivan f
reviewing the histology, Mr John Hynd for carrying o
the excellent anaesthesia, the Clinical Laboratory st
for their help and the St George's Hospital Resear
Fund for financial support. R. B. Ellis-Pegler is
receipt of a research grant from the Wellcome Tru

References

ARTZ C. P., BARNETT W. O. and GROGAN J. B. (196
Further studies concerning the pathogenesis a
treatment of peritonitis. *Ann. Surg.* **155**, 75
766.

BOWER J. O., BURNS J. C. and MENGLE H. A. (193
Induced spreading peritonitis complicating ac
perforative appendicitis. *Surg. Gynecol. Obst*
66, 947–961.

BROWNE M. K. and STOLLER J. L. (1970) Intraperiton
noxythiolin in faecal peritonitis. *Br. J. Surg.*
525–529.

BURNETT W. E., BROWNE G. R., ROSEMOND G.
CASEWELL H. T., BUCHER R. B. and TYSON R.
(1957) The treatment of peritonitis using pe
toneal lavage. *Ann. Surg.* **145**, 657–681.

CROOK J. N., COTLAR A. M., BORNSIDE G. H. and COH
(1968) Intraperitoneal cephalothin in the tre
ment of experimental appendiceal peritoni
Am. Surg. **34**, 736–739.

ELLIS-PEGLER R. B., CRABTREE C. and LAMBERT H.
(1975) To be published.

FILLER R. M. and SLEEMAN H. K. (1967) Pathogenesis
peritonitis. 1. The effect of *Escherichia coli* a
hemoglobin on peritoneal absorption. *Surgery*
385–392.

HAWKSWORTH G., DRASER B. S. and HILL M. J. (19
Intestinal bacteria and the hydrolysis of glyc
sidic bonds. *J. Med. Microbiol.* **4**, 451–459.

HYND J. (1975) To be published.

LAVIGNE J. E., BROWN C. S., MACHIEDO G. W., BLAC
WOOD J. M. and RUSH B. F. (1974) The treatme
of experimental peritonitis with intraperiton
Betadine solution. *J. Surg. Res.* **16**, 307–311.

PICKERSGILL J. and ELLIS-PEGLER R. B. (1975) To
published.

SCHUMER W., LEE D. K. and JONES B. (1964) Periton
lavage in postoperative therapy of 'late peritone
sepsis. Preliminary report. *Surgery* **55**, 84
845.

SILVANI H. L., ROTHENBERG S., WARMER H., AMLUXEN
and MCCORKLE H. J. (1947) Laboratory and clini
experiences with Streptomycin therapy in t
management of infections of intestinal orig
Surg. Gynecol. Obstet. **85**, 721–726.

WILLIAMS-SMITH H. (1965) Observations on the fl
of the alimentary tract of animals and fact
affecting its composition. *J. Pathol. Bacteriol.*
95–122.

ZINTEL H. A., ZINSSER H. H., RUNYON W., JACKSON G.
NICHOLS A. C., WILEY M. M. and WILLIAMS W.
(1950) Influence of antibiotics and sulfonami
on the mortality and bacteria of experimen
peritonitis. *Surg. Gynecol. Obstet.* **91**, 742–750.

Br. J. Surg. Vol. 62 (1975) 645–646

The effect of noxytiolin in experimental peritonitis

D. W. KING, J. F. GURRY AND B. N. BROOKE*

SUMMARY

The evidence for the value of noxytiolin (Noxyflex) in peritonitis is contradictory. In a controlled trial of the effect of noxytiolin in peritonitis in rabbits we have found a significant increase in mortality in the trial group compared with a control group, but no significant difference when a dose equivalent to the recommended human dose is used. The postoperative course is adversely affected in the animals receiving noxytiolin.

NOXYTIOLIN (Noxyflex, Geistlich) has gained acceptance as a therapeutic agent in peritonitis with little objective evidence of its value. It has a different chemical structure from other antibacterial or antimycotic agents and its mode of action has not been determined. A possible explanation of its action is its chemical similarity with methyl-mustard oil, which has a considerable Gram-positive and Gram-negative antibacterial spectrum due to transaminase inhibition. Another theory is that intact noxytiolin may penetrate the bacterial cell membrane and dissociate intracellularly into methyl-thiourea and formaldehyde.

According to Browne and Stoller (1970) intraperitoneal injection of noxytiolin offered significant protection against a lethal Gram-negative peritonitis induced with proteus and coliform organisms in guinea-pigs. They also presented a series of patients with faecal peritonitis with a low mortality rate, thought to be due, in part at least, to an instillation of 2·5–5·0 g into the peritoneal cavity at the time of operation.

However, Cleaver et al. (1974) were unable to show that lavage with noxytiolin was more beneficial than with Hartmann's solution in faecal peritonitis in rats.

We have performed a controlled trial of the effect of noxytiolin in experimental peritonitis in rabbits.

Materials and methods

Peritonitis was induced in 40 New Zealand White rabbits by the method previously described (p. 642 of this Journal), with 35 survivors which were treated as follows. At the time of appendicectomy either nothing further was done or 5 ml of one of the following solutions were instilled into the peritoneal cavity: normal saline, 2·5 per cent noxytiolin or 10 per cent noxytiolin, the noxytiolin being mixed immediately before administration. Thus, control and trial groups were obtained (*Table I*). The animals were weighed at the same time each day.

Results

The mortality for each group is shown in *Table I*; it was higher in the rabbits receiving noxytiolin, the difference between the trial and control groups being significant at the 5 per cent level (Fisher's exact probability test).

The 3 deaths in the control group occurred on the second postoperative day, but in the noxytiolin group while 7 died during the second postoperative day, the remaining 3 deaths occurred later, between the eighth and eleventh postoperative days. At autopsy all had diffuse purulent peritonitis; this had become walled off into abscess cavities in those dying after 7 days and in those surviving for 2 weeks.

A greater postoperative weight loss was seen in the trial group compared with the controls, and this is significant ($P < 0·01$) when subjected to the sign test and analysis of variance (Seigal, 1956) (*Fig.* 1). The 13 rabbits dying postoperatively are excluded; those dying in the first 2 days lost weight at the same rate as the rest, but those dying later lost more weight generally, falling as low as 67 per cent of the preoperative weight in two instances.

A comparison of peripheral blood levels of noxytiolin every 15 minutes for 1 hour following instillation of 5 ml of 10 per cent noxytiolin into a normal rabbit and one with peritonitis revealed an increased absorption of noxytiolin in peritonitis (*Fig.* 2). No significant blood levels could be detected following instillation of 2·5 per cent noxytiolin.

Table I: WEIGHT AND MORTALITY

Instillation	Group	No. surviving periop. period	Average preop. weight (g)	Mortality	
				No.	%
—	Control	8	3139	1	12·5
5 ml N saline		9	2583	2	22·2
	Total	17	2845	3	17·6
5 ml 2·5% noxytiolin		10	2882	5	50
5 ml 10% noxytiolin		8	2624	5	62·5
	Total	18	2768	10	55·6

Discussion

The evidence of the benefits of noxytiolin is contradictory; only Browne and Stoller (1970) have demonstrated any protection from peritonitis in experimental animals. The evidence of its benefits in clinical peritonitis comes largely from uncontrolled trials (Browne and Stoller, 1970; Pickard, 1972). We are at present conducting a double blind clinical trial in perforated appendicitis.

The dose of 5 ml of 2·5 per cent noxytiolin corresponds approximately to the recommended dose in

---

* Department of Surgery, St George's Hospital, London.
Present address of D. W. King: St Mark's Hospital, London.

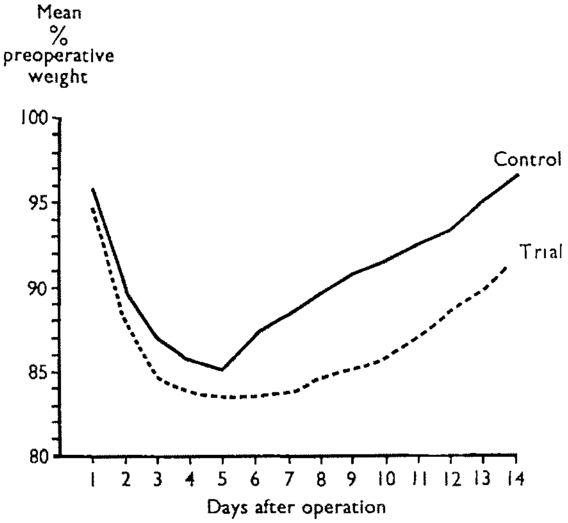


Fig. 1. Postoperative weight changes of the experimental group compared with those of the controls.

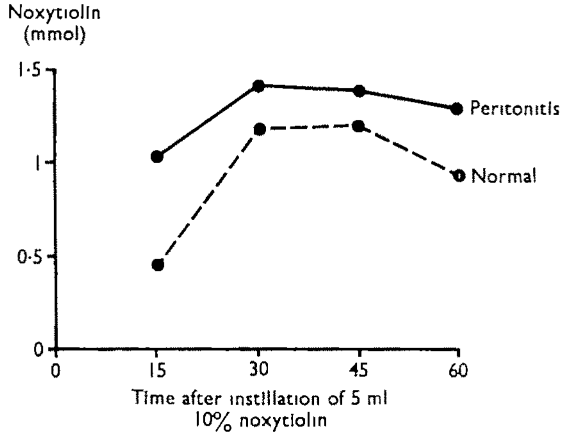


Fig. 2. Comparison of peripheral blood levels of noxytiolin after instillation of 5 ml of 10 per cent noxytiolin in a normal rabbit and in one with peritonitis.

humans of 100 ml of 2·5 per cent noxytiolin in adults. Compared with the control group there was a significant increase in mortality in the trial group, half of which received the recommended therapeutic dose and the other half of which received a higher dose. Though the higher dose did not significantly increase the mortality (*Table I*), it appears that toxicity increases *pari passu* with dosage, judging by weight loss (*Fig.* 3), which may possibly be attributable to the breakdown of the drug to methyl-thiourea and formaldehyde in the body. Browne and Stoller (1970) have shown that intraperitoneal injection of noxytiolin thrice weekly for 3 weeks in high doses produces patchy bronchopneumonia and cloudy swelling of the liver in Wistar rats. Moreover, the presence of peritonitis increases absorption (*Fig.* 2).

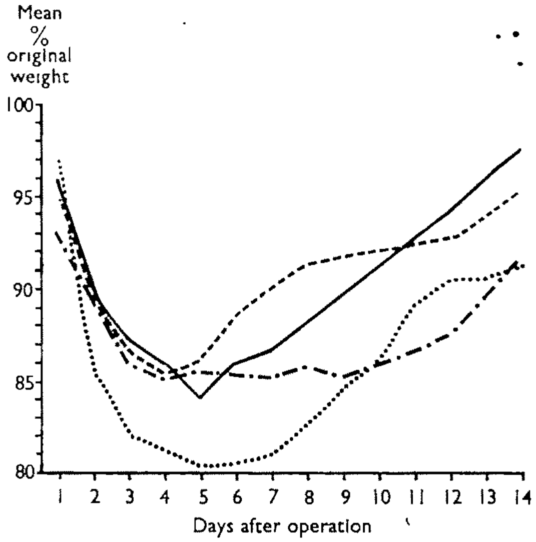


Fig. 3. Postoperative weight changes in the four groups:
——, no instillation; – – –, 5 ml of normal saline;
–·–·, 2·5 per cent noxytiolin; ········, 10 per cent noxytiolin.

Conclusion

Noxytiolin significantly increased the mortality in rabbits due to peritonitis from perforated appendicitis. There was also a significantly greater weight loss among the surviving rabbits of the trial group compared with the controls, which may be attributable to the increased absorption of the drug in peritonitis.

Acknowledgements

We would like to thank Dr I. Brown for estimating noxytiolin levels, Mr John Hynd for carrying out the anaesthesia, Miss M. Leighton of St Bartholomew's Hospital for statistical advice and the St George's Hospital Research Fund for financial support.

References

BROWNE M. K. and STOLLER J. L. (1970) Intraperitoneal noxytiolin in faecal peritonitis. *Br. J. Surg.* **57**, 525–529.

CLEAVER C. L. T., HOPKINS A. D., KEE KWONG K. C. and RAFTERY A. T. (1974) The effect of postoperative peritoneal lavage on survival peritoneal wound healing and adhesion formation following faecal peritonitis: an experimental study in the rat. *Br. J. Surg.* **61**, 601–604.

PICKARD R. G. (1972) Treatment of peritonitis with pre- and postoperative irrigation of the peritoneal cavity with noxythiolin solution. *Br. J. Surg.* **59**, 642–648.

SEIGAL S. (1956) *Non-parametric Statistics for the Behavioural Sciences.* International Student Edition. London, McGraw-Hill, p. 68.

Br. J. Surg. Vol. 62 (1975) 647–650

Results of modified Robert Jones operation for clawed hallux

E. I. M'BAMALI*

SUMMARY

The results of modified Robert Jones operation for clawed hallux carried out on 36 feet were reviewed by clinical and radiological investigations. Twenty-nine feet (80 per cent) achieved good results while 3 feet (8·5 per cent) obtained fair results and in 4 feet (11 per cent) the results were poor. Better results were obtained in the poliomyelitis cases than in the other groups.

Correction of deformity appears to be achieved by the transferred extensor hallucis longus elevating the first metatarsal neck and by the flexor hallucis longus flexing the rigid toe obtained by interphalangeal arthrodesis.

Tendon regeneration which is associated with recurrent clawing remains a problem.

Internal fixation should be used for the interphalangeal arthrodesis.

CLAW toes with dorsal subluxation or dislocation of the metatarsophalangeal joints may be associated with painful callosities and disability unrelieved by conservative measures. In 1916 Robert Jones described an operation to correct this deformity in which the extensor hallucis longus was transferred to the first metatarsal neck, and it is now common practice to fuse the interphalangeal joint of the hallux as well. A review of the results of this operation carried out in Cardiff is presented here.

Patients

There were 26 patients treated between 1954 and 1968, thus providing a follow-up period of between 4 and 19 years, with an average of 10·9 years (*Table I*). There were 11 males and 15 females. Ten cases were bilateral whilst 16 had unilateral involvement, making a total of 36 feet available for review. Their ages at the time of operation ranged from 2 to 49 years, the average being 15 years. The majority of the patients were operated on in the second decade (*Fig.* 1). About half the cases (46 per cent) were secondary to poliomyelitis (*Table II*). The next biggest group was the idiopathic cases (38 per cent), while miscellaneous causes included 1 case each of Friedreich's ataxia, spastic hemiplegia, postmeningitic spasticity and congenital hemivertebra with scoliosis.

Table I: DETAILS OF THE PRESENT SERIES

No. of cases	
Unilateral	16
Bilateral	10
Total	36
Age (yr)	
Range	2–49
Average	15
Sex	
Male	11
Female	15
Period of follow-up (yr)	
Range	4–19
Average	10·9
Tendon regeneration	
Unilateral	3
Bilateral	3
Total	9

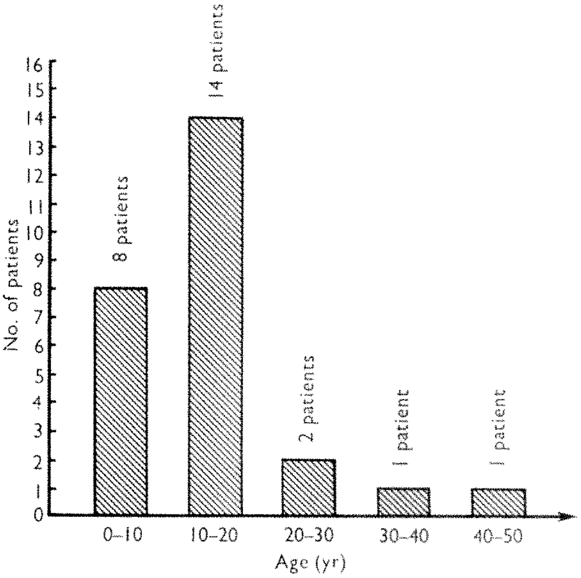


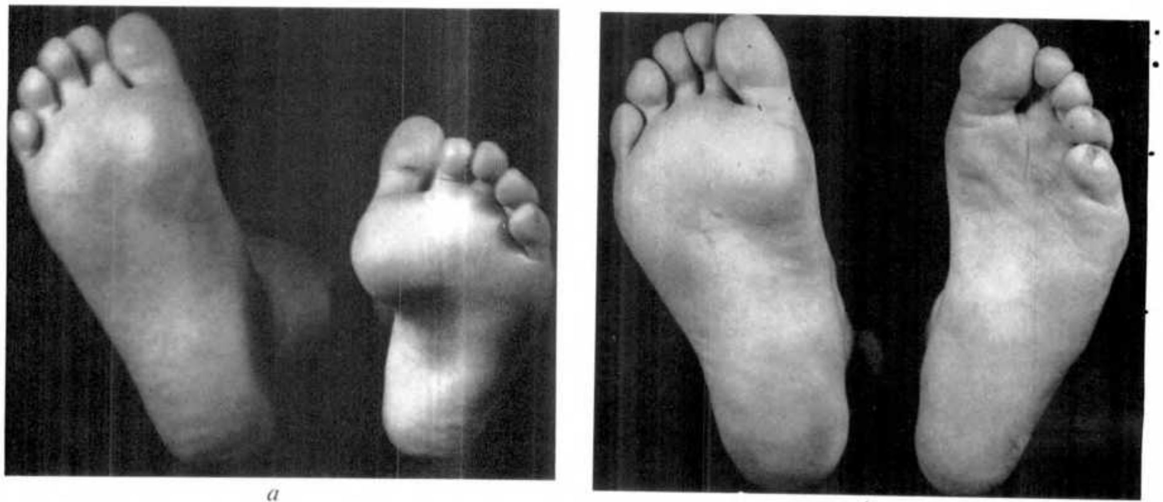
Fig. 1. No. of operations performed in each decade.

Operative method

The method used was standard. An L-shaped dorsal incision was used. The long extensor to the hallux was divided close to its insertion in the base of the distal phalanx. The interphalangeal joint was then arthrodesed by excising the articular cartilage of the phalanges, opposing the denuded surfaces and holding them fixed with catgut stitches passed through the remnants of the long extensor distally and the capsule proximally. No internal fixation was used. The proximal fragment of the divided long extensor tendon was then passed through a drill hole in the neck of the first metatarsal and sutured back to itself with the ankle in full extension. The foot was immobilized in a below-knee plaster for between 8 and 12 weeks.

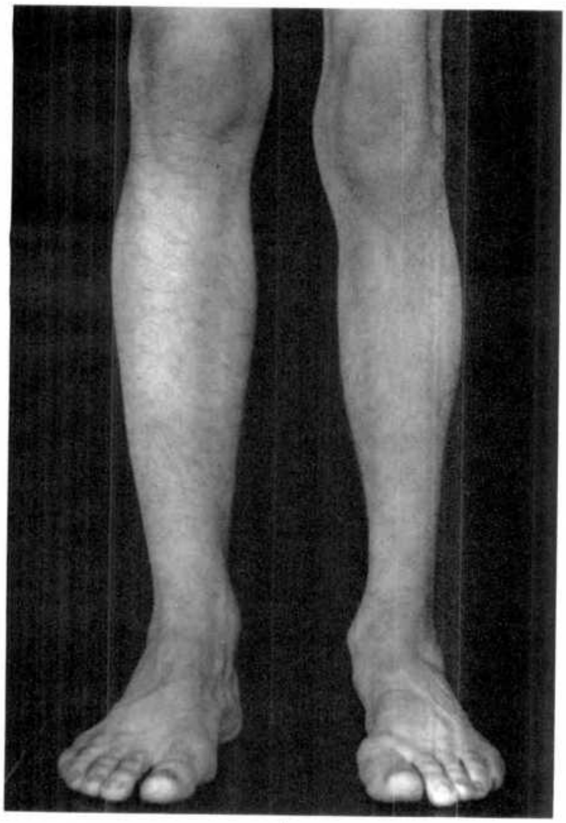
---

* Department of Orthopaedic Surgery, University Hospital of Wales, Cardiff. Present address: Battle Hospital, Reading.



a

b



c

Fig. 2. *a*, Clawed deformity of left hallux before operation. *b*, After operation. Clawing of the hallux has been corrected and the result is good. *c*, After operation with the patient standing. The good correction is maintained on weight bearing.

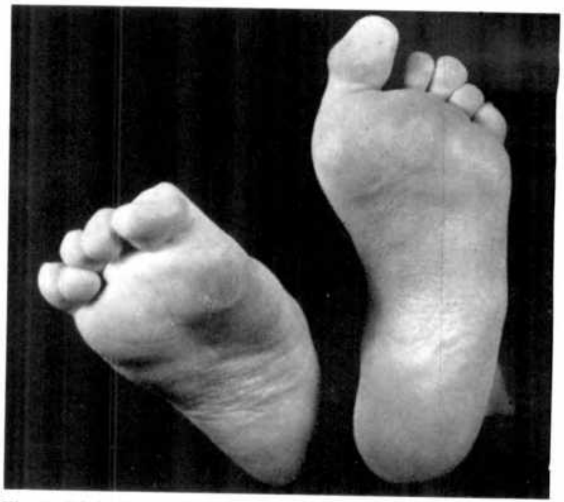


Fig. 3. Right hallux after operation demonstrating a poor result. Note the clawing of the hallux and the callosity over the first metatarsal head.

Table II: AETIOLOGICAL FACTORS

Aetiology	No. of cases	%
Poliomyelitis	12	46
Idiopathic	10	38
Miscellaneous		
Friedreich's ataxia	1	15
Spastic hemiplegia	1	
Postmeningitic hemiplegia	1	
Associated with congenital hemivertebra and scoliosis	1	

Total number of paralytic feet was 16 (poliomyelitis 12, miscellaneous 4) or 61 per cent.

Results

The primary aims of the operation are to correct deformity (clawing) and to relieve symptoms (pain, with or without callosities) in the hallux. The results based on the presence of postoperative deformity and symptoms were graded as follows:

Good: Deformity (clawing of the hallux) corrected and no symptoms.

Fair: Deformity not corrected but no symptoms.

Poor: Deformity not corrected and persistent symptoms present.

Using the above criteria 29 feet (80 per cent) obtained good results (*Table III*, *Fig*. 2), 3 feet obtained fair results and 4 feet (11 per cent) had poor results (*Table III*, Fig. 3). The age at operation or period of follow-up did not seem to affect the results.

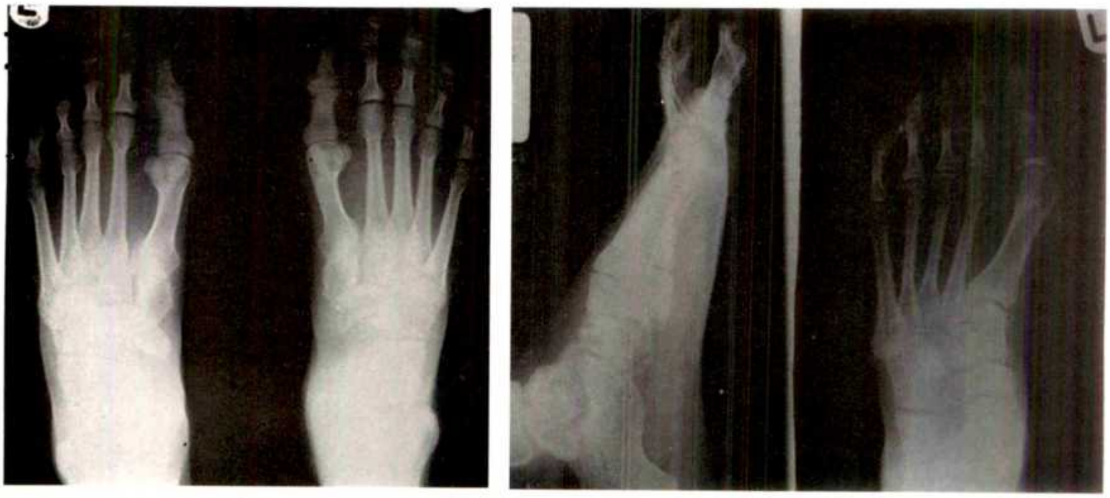

a
b

Fig. 4. *a*, X-ray showing bilateral fibrous union of the interphalangeal arthrodesis. *b*, X-ray illustrating bony union of an interphalangeal arthrodesis.

Table III: RESULTS OF OPERATION

Result	No. of feet	%
Good (no deformity or symptoms)	29	80
Fair (no symptoms but clawing recurred)	3	8·5
Poor (clawing with symptoms)	4	11

Table IV: INCIDENCE OF FIBROUS UNION AND MALUNION

Type	No. of feet
Fibrous union	
Unilateral	3
Bilateral	4
Total	11 (31%)
Malunion	
In flexion alone	6
In medial rotation alone	6
In flexion and medial rotation	3
Total	15 (42·5%)

Five of the 29 feet classified as good results had symptoms from foot deformities unrelated to clawing of the hallux. These patients together with the 3 poor results were dissatisfied with the operation. In 7 feet (2 bilateral and 3 unilateral) clawing of the hallux had recurred. In 5 the extensor hallucis longus had regenerated. In 4 feet the persistent clawing was associated with both tendon regeneration and fibrous union of the interphalangeal arthrodesis.

In only 1 of the 7 feet with recurrent clawing was the aetiology poliomyelitis. In 3 the aetiology was unknown, while 1 was secondary to Friedreich's ataxia and 2 to spastic hemiplegia. Thus, better results were obtained in cases secondary to poliomyelitis.

Complications

Union of the interphalangeal arthrodesis

Seven patients developed fibrous union of the interphalangeal arthrodesis. Four were bilateral and 3 unilateral, making a total of 11 feet or approximately 31 per cent of all cases (*Table IV*, *Fig.* 4*a*). Union was bony in the rest (*Fig.* 4*b*). Only 1 case of fibrous union was symptomatic.

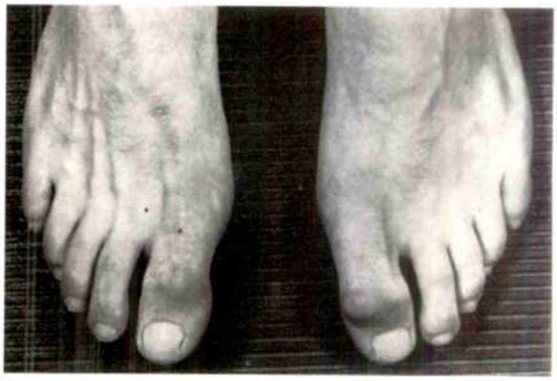


Fig. 5. Photograph demonstrating regeneration of the right extensor hallucis longus.

Malunion occurred in 11 patients, 4 bilaterally and 7 unilaterally. Thus, a total of 15 feet (42·5 per cent) had some degree of malunion (*Table V*). Malunion was in flexion in 6 feet, in medial rotation in 6 feet and in flexion with medial rotation in 3 feet. Three of the malunions in flexion developed asymptomatic adventitious bursae over the dorsum of the malunited interphalangeal fusion. In rotational malunions callouses developed on the volar surface of the medial side of arthrodesed interphalangeal joint. Thus, the sites of the adventitious bursae and callouses correspond to the points of pressure to be expected from the deformities. It is probably a question of time before painful symptoms develop at these sites as well.

Wound

There was no overt wound infection or early wound breakdown. Late wound complications included 2 cases of mild wound contractures and 1 case of hyperaesthesia of the wound and medial side of the hallux, presumably due to injury to the medial digital nerve at operation.

The metatarsophalangeal joint
All were examined radiologically and none showed any sign of osteo-arthritic changes. Clinically, only 1 of 18 feet examined showed stiffness of the joint.

Tendon regeneration
The extensor hallucis longus re-formed in 6 patients, 3 bilaterally, 2 on the left side and 1 on the right side. Thus, in a total of 9 feet (approximately 25 per cent of all cases) the tendon had regenerated (*Fig.* 5). This was associated with recurrent clawing in 5 feet (14 per cent).

Discussion

The results of this review show that a satisfactory result was obtained in 80 per cent, suggesting that it is a worthwhile procedure. The results were better in cases due to poliomyelitis than in other groups. From an analysis of the results it is possible to offer a comment on the mechanism by which correction is achieved. There are two possiblities. In the first, the transferred extensor hallucis longus tendon may act to elevate the first metatarsal neck as Robert Jones (1916) originally intended. Secondly, the addition of interphalangeal arthrodesis, apart from preventing flexion deformity of the interphalangeal joint, may also enhance correction of the clawing by achieving a rigid hallux upon which the long flexor tendon may act to reduce the extension of the metatarsophalangeal joint (Lambrinudi, 1938).

It would appear that both mechanisms were involved because, although there was a definite association between regeneration of the extensor tendon and recurrent clawing (the tendon had regenerated in 5 out of 7 feet with recurrent clawing), the fact that this was not invariably so when firm union of the interphalangeal fusion was achieved (in 4 cases out of 9) suggests that the second mechanism is also important.

It is obviously desirable that regeneration of the tendon should be minimized, and the technique of Ledge tenodesis described by Kirk et al. (1971) could possibly be adopted.

Fibrous union of the interphalangeal arthrodesis was also a problem in this series and although this was not often productive of symptoms in itself, because of its importance in helping to reduce the deformity, it would seem wise to adopt the technique of internal fixation with a medullary wire as suggested by O'Donoghue and Stauffer (1943).

Acknowledgements

I am indebted to Professor B. McKibbin for his help and advice in preparing this manuscript. I am grateful to Mr H. J. Richards and the late Mr Dylwyn Evans for allowing me to study their patients. I also wish to thank Mr C. Walker for the illustrations, and Mrs M. Hart and Miss C. Antonucci for their secretarial work.

References

JONES R. (1916) The soldier's foot and the treatment of common deformities of the foot. Part II. *Br. Med. J.* **1**, 749.

KIRK A. A., KUNKE H. M. and WAIVE H. J. (1971) Ledge tenodesis of extensor hallucis longus. *J. Bone Joint Surg.* **53A**, 774.

LAMBRINUDI C. (1938) Functional aspect: action of the foot muscles. *Lancet* **2**, 1480.

O'DONOGHUE D. H. and STAUFFER R. (1943) An improved method for obtaining body fusion of the great toe. *Surg. Gynecol. Obstet.* **67**, 498.

Br. J. Surg. Vol. 62 (1975) 651–652

Lymphosarcoma of the breast

CHARLES F. ROSS AND ARNOLD ELEY*

SUMMARY

A case of lymphosarcoma presenting as a breast tumour in a 68-year-old woman is described and the condition briefly reviewed.

IT is unusual for lymphosarcoma to present as a breast lump. The tumour reported here was at first thought to be primary, but the patient eventually died with generalized disease, as do the majority of patients with lymphosarcoma.

Case report

Mrs E. E., aged 68 years, presented with a lump in the lower quadrant of the right breast which she had first noticed 2 weeks before. On examination it was thought to be a carcinoma. No axillary lymph nodes were palpable and a simple mastectomy was done (A. E.) on 14 September 1966.

The pathology report (C. F. R.) was as follows: 'Simple mastectomy specimen 19×15×7 cm with a skin ellipse 19×10 cm bearing a normal nipple. An incision has been made into a firm, slightly lobulated, well-demarcated tumour, 3 cm diameter. On slicing, it is pinkish-grey and fleshy.'

It was thought to be a medullary carcinoma but microscopically proved to be a well-differentiated lymphosarcoma composed of mostly mature small lymphocytes, with a suggestion of follicular arrangement in places and invasion of the surrounding breast (*Fig.* 1). In some parts there was a good deal of fibrosis, with thick almost acellular bands. It was considered to be of low malignancy.

Exactly 2 years later the patient developed a subcutaneous lump over the left hip which macroscopically and microscopically closely resembled the breast tumour except that follicle formation was a little more evident and collagen less evident.

The patient continued in good general health, with a normal blood picture and no radiological evidence of dissemination until June 1971, when she developed an enlarged lymph node in the left groin. Histologically, the tumour was now anaplastic and resembled reticulum cell sarcoma, with much collagen formation (*Fig.* 2).

The patient was referred to Dr W. F. White at the Regional Radiotherapy Centre, St Luke's Hospital, Guildford, and was started on a course of chlorambucil 5 mg daily. She remained in good general health and chemotherapy was stopped in March 1972. The patient then moved from the district and remained well until the end of 1973, when she was found to have gross hepatomegaly, and chemotherapy was restarted. In spite of the latter the patient quickly deteriorated and died of bronchopneumonia on 4 July 1974. Necropsy (Dr G. B. Forbes) revealed an undifferentiated malignant lymphoma in the liver and spleen but no deposits elsewhere. The sections showed an appearance closely resembling that in *Fig.* 2.

Discussion

Sixty-eight cases of primary lymphosarcoma of the breast had been reported up to 1966, and Jernstrom and Sether (1967) described 3 further examples. Since then 50 more cases have been reported (Bellone, 1968; Boscaino et al., 1969; Yoshida, 1970; Freedman et al., 1971; Matsuyama et al., 1972; Seth et al., 1972; Wiseman and Liao, 1972; Case, 1973; Talvalkar, 1973). Freeman et al. (1972), in a paper considering extranodal lymphomas reported from 100 hospitals in the United States, had encountered 33 breast lymphomas in 1467 patients without disseminated disease when first seen. Haagensen (1971) had encountered 9 cases of the condition, and the total number now on record would appear to be 164 including that under discussion.

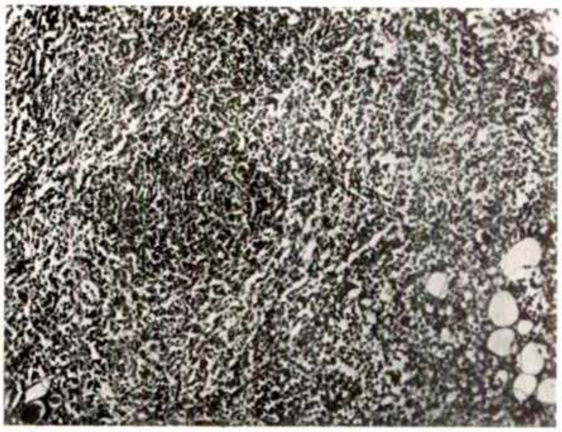


Fig. 1. Section of breast tumour. HE. (×106.)

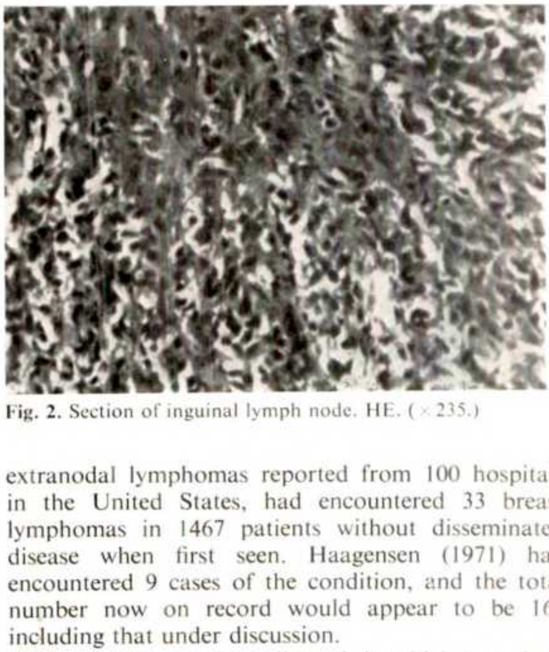


Fig. 2. Section of inguinal lymph node. HE. (×235.)

The disease may be unilateral, in which case there may be a single or several tumour nodules, or it may diffusely invade both breasts. A pregnant African Negress was recently described as having Burkitt's tumour affecting both breasts (Bannerman, 1966), but a similar condition has been reported outside Africa (Kay, 1955). When the tumour is solitary there is nothing to distinguish it clinically from carcinoma, but when a breast with several tumour nodules is encountered the possibility of lymphosarcoma should be considered. There is a definite predilection for the right breast. The age incidence is the same as that for carcinoma. The majority are in women and form about 0·2 per cent of malignant breast tumours in the female. Very few instances have been recorded in the male. A tumour nodule on one side may, after a period of many years, be followed by a similar lesion in the contralateral breast. Freedman et al. (1971) stated that bilaterality does not worsen the chances of survival.

---

* North West Surrey District Laboratory and Department of Surgery, St Peter's Hospital, Chertsey, Surrey.

Histologically, the growth may be well differentiated, as in the present case initially, or exhibit a varying degree of primitiveness through lymphoblastic to reticulum cell sarcoma. More than half the patients have involved axillary lymph nodes when first seen, but their presence and the size and number of tumours do not appear to be related to prognosis. The latter depends on the histological type, being best with lymphocytic and worst with reticulum cell sarcoma. It seems that the outlook is much better in lymphosarcoma than carcinoma whatever the treatment.

It is, of course, often difficult to know whether one is dealing with a primary or a secondary lesion, since sooner or later most of these patients have recurrences and it is impossible to be sure whether the original breast lesion is not the initial manifestation of a more generalized disease. However, it is distinctly uncommon for the latter to involve breast tissue (Milne and Maxwell, 1970) except in rapidly progressive lymphosarcomatosis occurring in pregnancy and the puerperium. In the more usual form of malignant lymphoma the natural history is quite different. Nevertheless, it appears that certain rare cases in which the breast is at first affected can be cured by mastectomy and the lesion is presumably arising as a primary in that organ.

Acknowledgements

Our thanks are due to Drs W. F. White, S. R. Drake (Kent and Canterbury Radiotherapy Centre) and G. B. Forbes (Kent and Canterbury Department of Pathology) for information regarding the treatment and subsequent course and for sections of the liver and spleen.

References

BANNERMAN R. H. O. (1966) Burkitt's tumour in pregnancy. *Br. Med. J.* **2**, 1136–1137.

BELLONE F. (1968) Una rarissima patologia mammaria: il linfosarcoma primitivo bilaterale. Descrizione di un caso. *Riv. Ital. Ginecol.* **52**, 750–751.

BOSCAINO N., GAMBARDELLA P. and PISCICELLI I. (1969) Contributo allo studio dei tumori linformatosi primitivi della mammella. *Acta Chir. Ital.* **25**, 359–371.

CASE T. C. (1973) Primary lymphosarcoma of the breast in a 75-year-old woman: case report. *J. Am. Geriat. Soc.* **21**, 235–238.

FREEDMAN S. I., KAGAN A. R. and FRIEDMAN N. B. (1971) Bilaterality in primary lymphosarcoma of the breast. *Am. J. Clin. Pathol.* **55**, 82–87.

FREEMAN C., BERG J. W. and CULTER S. J. (1972) Occurrence and prognosis of extranodal lymphomas. *Cancer* **29**, 252–260.

HAAGENSEN C. D. (1971) *Diseases of the Breast*, 2nd ed. London, Saunders.

JERNSTROM P. and SETHER J. M. (1967) Primary lymphosarcoma of the mammary gland. *JAMA* **201**, 503–506.

KAY S. (1955) Lymphosarcoma of female mammary gland. *Arch. Pathol.* **60**, 575–579.

MATSUYAMA M., SUCHI T., KURITA S., SATO T., SUZUKI H., TAKAGI I., MURAKAMI M. and TAKEUCHI S. (1972) Reticulum cell sarcoma of the breast—an autopsy case with terminal leukemic manifestation. *Acta Pathol. Jap.* **22**, 185–194.

MILNE R. M. and MAXWELL B. M. (1970) Lymphosarcoma of the female breast. *J. R. Coll. Surg. Edinb.* **15**, 38–40.

SETH H. N., RAY N. and BARAT A. K. (1972) Lymphosarcoma of female breast. Report of a case of primary breast lesion. *Indian J. Pathol. Bacteriol.* **15**, 122–124.

TALVALKAR G. V. (1973) Primary lymphosarcoma of the breast: A report of ten cases. *Indian J. Cancer* **10**, 322–329.

WISEMAN C. and LIAO K. T. (1972) Primary lymphoma of the breast. *Cancer* **29**, 1705–1712.

YOSHIDA Y. (1970) Recticulum cell sarcoma of breast. Case report and review of the Japanese literature. *Cancer* **26**, 94–99.

Br. J. Surg. Vol. 62 (1975) 653–667

Surgical Research Society

The 21st Anniversary Meeting of the Surgical Research Society was held at Southampton on 10, 11 and 12 July 1975 with Professor A. P. M. Forrest (President of the Surgical Research Society) in the chair. The following papers were presented:

1. The effect of meat extract stimulation on serum gastrin of patients undergoing proximal gastric vagotomy alone (PGV) and with Finney pyloroplasty (PGVP)

W. H. S. PIGOTT (C. WASTELL), *Department of Gastroenterology and Surgical Unit, Westminster Hospital, London*

Serum gastrin concentration may be elevated when the gastric antrum is stimulated by food retained within the stomach. Fasting and Oxo-stimulated serum gastrin levels have been measured by means of radio-immunoassay in patients following (range 4–39 months, mean 25 months) PGV and PGVP in 19 and 23 male patients respectively.

The fasting levels after PGV and PGVP were 57·9±48·8 and 62·7±42·1 and the peak levels were 131·1±65·0 and 123·9±71·3 respectively (all values mean±s.d. pmol/l). No significant difference in either these levels or the shape of the gastrin response could be shown between PGV and PGVP.

Five patients, 1 following PGV and 4 following PGVP, with proved recurrent ulcers were also studied. Four of these had serum gastrin values similar to those found in patients without recurrence, but the fifth, who had a pyloroplasty, had hypergastrinaemia with a fasting level of 170 pmol/l and a peak level of 390 pmol/l. Antrectomy in this patient almost removed detectable serum gastrin to Oxo stimulation.

It is concluded that PGV does not result in either higher fasting or peak serum gastrin levels than PGVP and that although some recurrent duodenal ulcers are associated with elevated serum gastrin, the majority are not.

2. The treatment of superficial thrombophlebitis: a randomized double blind study using local heparinoid cream

P. P. MEHTA, S. SAGAR and V. V. KAKKAR, *Department of Surgery, King's College Hospital Medical School, London*

Superficial thrombophlebitis is a common complication of continuous intravenous infusion. Heparinoid cream (mucopolysaccharide polysulphate) has been shown to be absorbed into the circulation when applied to the skin and to produce a heparin-like action on blood clotting.

One hundred patients who developed infusion thrombophlebitis were randomly allocated to receive heparinoid or placebo cream for 5 days. The limbs were examined every day and changes in the local signs of thrombophlebitis recorded. The ^{125}I-fibrinogen test was used for quantitative assessment of the fate of the thrombus, and radioactivity at the site of thrombophlebitis was recorded every day for 5 days. Fifty of the 100 patients included received the placebo cream and 50 the heparinoid cream. The mean time required for the relief of local symptoms and signs in the placebo group was 126 hours (range 48–148 hours) while in the heparinoid group it was 58 hours (range 36–102 hours). The decline in percentage radioactivity in the two groups was as follows:

% Radioactivity

	Placebo group		Heparinoid group	
Day	Mean	Range	Mean	Range
1	100		100	
2	135·4	66–280	85·5	45–135
3	116·1	24–224	58·9	10–120
5	76·3	24–192	23·5	5–60

These results suggest that local application of heparinoid cream produces symptomatic improvement and assists in early resolution of thrombophlebitis.

3. Renal function before and after haemorrhage in rats with chronic bile duct obstruction: a micropuncture study

N. E. MOSS, MARY FRASER, C. J. RYAN, A. C. KENNEDY, MARJORIE E. M. ALLISON and L. H. BLUMGART, *University Departments of Surgery and Medicine, Glasgow Royal Infirmary*

In rats with biliary tract obstruction, renal ischaemia is consistently followed by severe acute renal failure (Dawson, 1964).

We have used micropuncture and light and electron microscopy techniques to study single nephron and whole kidney structure and function before and immediately after haemorrhagic shock in rats with chronic bile duct obstruction and in sham-operated control rats.

In vivo the kidneys of rats with common bile duct obstruction appeared abnormal, with deposition of pigment throughout the renal tubule cells and with intratubular debris and pigment. Urine flow rate, sodium excretion, whole kidney glomerular filtration rate, superficial single nephron filtration rate, glomerular capillary hydrostatic pressure and proximal fractional reabsorption were not significantly different in the two groups before haemorrhage. Renal plasma flow, however, was significantly increased and filtration fraction significantly decreased in rats with common bile duct obstruction. Free flow proximal intratubular hydrostatic pressure varied in the rats with an obstructed common bile duct (6–34 mm Hg), high pressures presumably being due to distal intratubular block.

Haemorrhage to 30 mm Hg for 30 minutes and retransfusion resulted in a significant diuresis and natriuresis, more marked in the control rats, but without a significant change in blood pressure or haematocrit. The superficial single nephron filtration rate fell significantly in both groups but especially in the jaundiced animals where there was also a parallel fall in glomerular filtration rate and renal plasma flow. No change in proximal fractional reabsorption was found. Hence, factors operating beyond the proximal tubule must be important in the diuretic response.

We conclude that chronic bile duct obstruction in the rat results in structural changes and subtle alteration in renal function with evidence of tubular obstruction, and that the response to haemorrhage is attenuated in these animals.

DAWSON J. L. (1964) Jaundice and renal anoxic damage. Protective effect of mannitol. *Br. Med. J.* 1, 810–811.

4. Blood viscosity studies in patients with Raynaud's syndrome

K. B. GOYLE and J. A. DORMANDY, *St James's and St George's Hospitals, London*

Whole blood and plasma viscosity measurements were carried out at 37 and 27 °C in 10 patients with Raynaud's syndrome as well as 10 normal controls. The Wells-Brookfield and the newly developed Contraves viscometers were used, which allowed measurements of viscosity to be made at a much wider range of shear rates than had hitherto been possible (from 0·7 to 230/sec). The patients were also assessed clinically, biochemically and by histological examination of full thickness skin biopsies from a finger pulp. The results at 37 °C were consistent and showed a small but significant increase in the relative viscosity of the patients' blood compared with the controls. More importantly, lowering the temperature to 27 °C increased the abnormality in the patients' blood considerably.

At 27 °C the mean blood viscosity, measured at a shear rate of 0·77/sec, of patients with Raynaud's syndrome was 22·5 ± 2·9 (s.d.) c.p.s. The comparable value for normal controls was 16·7 ± 2·6 c.p.s. (The difference has a P value of 0·05.)

These results suggest that the periodic digital circulatory insufficiency in patients with Raynaud's syndrome may be due to an abnormal increase in blood viscosity locally which is precipitated by a fall in tissue temperature.

5. Treatment of Raynaud's syndrome with stanozolol

P. E. M. JARRETT, M. MORLAND, G. CLEMENSON and N. L. BROWSE, *Department of Surgery, St Thomas's Hospital, London*

Patients with scleroderma and Raynaud's disease have been shown to have lowered blood fibrinolytic activity (Cunliffe and Menon, 1969). We have studied the effect on such cases of stanozolol, which enhances natural fibrinolysis.

Twenty patients have had their clot weight fibrinogen, dilute blood clot lysis time (DBCLT), plasma fibrinolytic activity (fibrin plate) and hand blood flow (volume displacement plethysmography) measured before and after 3 months of treatment with stanozolol tablets 5 mg b.d.

Fourteen patients completed the course and had no intercurrent operation or illness. Eighty per cent felt that their hands were warmer and they were having fewer Raynaud's attacks. All wished to start a second course of treatment after being off the tablets for 1–2 months. Eleven have recommenced treatment following 3 months without stanozolol.

	DBCLT (min)	Fibrin plate (mm^2)	Clot weight fibrinogen (mg/100 ml plasma)	Hand blood flow (ml/min $100\ ml^{-1}$)
Before stanozolol	417	385	387	5·5
After 3 months of stanozolol	176	371	258	10·8
Significance of change P (t-test)	0·01	0·87	0·001	0·001

The results after 3 months off treatment and a second 3 months of treatment will be reported.

These results show that enhancement of fibrinolysis and reduction of plasma fibrinogen induced by stanozolol may be beneficial in scleroderma and Raynaud's disease.

CUNLIFFE W. J. and MENON I. S. (1969) Blood fibrinolytic activity in diseases of small blood vessels and the effect of low molecular weight dextran. *Br. J. Dermatol.* **81**, 220–225.

6. Comparison of pituitary function and clinical response after transphenoidal and transfrontal hypophysectomy for advanced breast cancer

T. BATES, R. D. RUBENS, R. D. BULBROOK, P. R. GOODWIN, D. Y. WANG, M. A. FALCONER, L. F. W. SALMON, P. H. SCHURR, O. H. SHAHEEN, R. K. KNIGHT and J. L. HAYWARD, *Imperial Cancer Research Fund Breast Cancer Unit, Guy's Hospital, London*

Transphenoidal hypophysectomy has been introduced as an alternative to the transfrontal operation for advanced breast cancer. The effect of these two operations on endocrine function has been compared.

Pituitary stimulation tests were carried out before and 10 days and 6 weeks after hypophysectomy. Ten patients had a transfrontal and 10 patients a transphenoidal operation. Thyrotrophin-releasing hormone (TRH) 400 μg and gonadotrophin-releasing hormone (LH-FSH-RH) 200 μg were given intravenously, and plasma FSH, TSH and prolactin (HPr) were measured at 0, 20, 30 and 60 minutes. Basal blood ketosteroids (DS and AS) were also determined.

After transfrontal hypophysectomy basal FSH, TSH, DS and AS concentrations were extremely low in the majority of patients and did not increase after stimulation. HPr levels were in the high normal range and in 2 cases there was a marked response to stimulation.

After transphenoidal hypophysectomy hormone levels were generally higher (2–10 times) than after the transfrontal operation, and stimulation led to marked increases in 8 of 10 cases. Basal HPr levels were again in the high normal range.

There were a similar number of clinical remissions in both groups but hormone levels did not appear to correlate with clinical response.

7. Oestrogen receptor activity in human breast tumours

R. A. HAWKINS, A. HILL, E. KILLIN, I. SMITH, M. MAUREEN ROBERTS, A. R. CURRIE and A. P. M. FORREST, *Departments of Clinical Surgery and Pathology, University of Edinburgh*

Oestrogen receptor activity has been determined by saturation analysis in 164 tissues. Activity was detected in 98 of 140 malignant breast tumours, whether primary or metastatic. The range of binding sites was 0·1–77·2 fmol/mg and the dissociation constant of binding 0·15–1·5 M.

Receptors were present in 5 of 24 benign breast tissues; in only one, a giant fibro-adenoma, was activity high (8·5 fmol/mg).

The incidence of receptor activity increased with experience and the concentrations were greater in postmenopausal than premenopausal women.

To determine if estimates were reproducible within a single tumour 10 large tumours were specially examined. Each was cut into sections, and two to three areas, the histology of which was defined, were selected for receptor assays. Although there was considerable variation in receptor concentration, averaging 2·3 times, there was no difference as far as the presence or absence of receptor activity was concerned. An oestrogen receptor assay on a single portion of tumour may have qualitative but not quantitative relevance.

8. Factors which influence the location of atherosclerosis. Is turbulence good or evil?

N. L. BROWSE, M. LEA THOMAS and A. E. YOUNG, *Department of Surgery, St Thomas's Hospital, London*

The disruption of streamlined flow at arterial bifurcations is commonly quoted as the reason for the high incidence of atherosclerosis at such sites, yet the most common site of atheromatous stenosis is the middle of the femoral artery at the adductor hiatus, where there is no bifurcation.

In a review of 50 arteriograms we found the external iliac, common femoral and lower popliteal arteries were least diseased. These segments cross joints.

We have measured the length and diameter of the popliteal artery across the extended and flexed knee joint by radiological and haemodynamic methods in 26 dogs. The artery shortens by 1·3 per cent/10° of flexion. The diameter does not change. Similar changes of length (2·2 per cent/10°) have been found during flexion of the knee and elbow in 11 men.

In a slow flow model, and in *in vivo* pulsatile flow, bending the vessels causes turbulence in the distal half of the bend.

We therefore postulate that repeated changes in length and turbulent flow keep the distal half of the external iliac and popliteal arteries free of atheroma. Atheroma occurs in bifurcations, the abdominal aorta, common iliac artery and adductor hiatus because these segments are fixed and flow is streamlined. Turbulence and movement are good not evil.

9. Early diagnosis of jaundice: a computer and clinical study

R. P. KNILL-JONES, K. M. COCHRAN, G. S. SOKHI, R. I. RUSSELL and L. H. BLUMGART, *University Department of Surgery and Gastroenterology Unit, Glasgow Royal*

Infirmary, and Department of Medicine in relation to Mathematics and Computing, University of Glasgow

Prospective studies have given encouraging results in the use of Bayesian statistics for the diagnosis of jaundiced patients (Knill-Jones et al., 1973). To evaluate their use further the system was studied prospectively on 40 patients from two specialist units with an interest in hepatic and biliary disease. A maximum of 60 items of routine clinical and laboratory data available within 48 hours of a patient's admission was collected on a standard form and the diagnosis was calculated by a computer program using likelihoods obtained from the earlier study. The accuracy was assessed by comparing the calculated 48-hour diagnosis of 1 of 11 diseases causing jaundice to the final agreed clinical diagnosis. In 16 patients the probability of the calculated diagnosis was $>0·96$ (accuracy 88 per cent), and in the remaining 24 patients with a lower probability the accuracy of diagnosis was 65 per cent. A simpler decision between a 'medical' or 'surgical' cause for jaundice in the same group of patients was also calculated and where the probability was $>0·96$ the diagnosis was correct in 27 out of 28 cases.

Although the computer diagnosis was no better than specialist diagnosis in this study, it has been shown to be more accurate than that of non-specialist clinicians (Stern et al., 1974), especially in situations where refined diagnostic facilities are lacking and there is a danger of early diagnostic laparotomy.

KNILL-JONES R. P., STERN R. B., GRIMES D. H., MAXWELL J. D., THOMSON R. P. H. and WILLIAMS R. (1973) Use of sequential Bayesian model in diagnosis of jaundice by computer. *Br. med. J.* **1**, 530–533.

STERN R. B., KNILL-JONES R. P. and WILLIAMS R. (1974) Clinician versus computer in the choice of 11 differential diagnoses of jaundice based on formalised data. *Methods Inf. Med.* **13**, 79–82.

10. The influence of two methods of haemostasis on the rate of wound sepsis: a random controlled trial of ligature and diathermy

R. S. ARNOT, MARY EVANS and A. V. POLLOCK, *Scarborough Hospital, Yorkshire*

Four hundred years ago Ambroise Paré found that sepsis was less likely to develop in wounds in which bleeding vessels had been ligated rather than cauterized (Hastings, 1974). The incidence of postoperative wound sepsis after haemostasis by ligature or diathermy has not previously been studied.

In consecutive patients 248 clean and 308 potentially contaminated general surgical operations were randomized for haemostasis either by ligature or diathermy. In clean wounds the incidence of primary wound sepsis was not influenced by the type of haemostasis, but secondary sepsis (after discharge of a wound haematoma) was significantly commoner when ties were used (12 out of 134 or 9 per cent, compared with 1 out of 114 or 0·9 per cent; $\chi^2 = 8·092$, $P<0·01$).

In potentially contaminated operations control of primary sepsis depends both on aseptic techniques and effective chemoprophylaxis. In the present series when an adequate topical antibiotic was used the method of haemostasis made no difference to the infection rate. When, however, such an antibiotic was not used, ligature of bleeding vessels in the abdominal wall was associated with significantly less sepsis than was diathermy (34 out of 162 or 21 per cent, compared with 46 out of 146 or 31·5 per cent; $\chi^2 < 4·49$, $P<0·05$).

HASTINGS P. (1974) *Medicine: An International History*. London, Benn.

11. Impaired lymphocyte protein synthesis in patients with glioma of the brain

D. G. T. THOMAS, CATHERINE LANNIGAN and P. O. BEHAN (B. JENNETT), *Department of Neurosurgery, Institute of Neurological Sciences, Glasgow*

Tumour-specific antigens have been demonstrated in glioma of the brain and there is evidence that patients can mount an immunological response to them (Wahlström et al., 1974); however, the prognosis of the condition is poor.

A study was made of lymphocyte protein synthesis in response to graded concentrations of phytohaemagglutinin (PHA) in short term, whole blood cultures (Pauly et al., 1973) of 9 patients with glioma of the brain and 8 with benign intracranial tumours (3 acoustic schwannöma, 5 meningioma). Forty-nine normal subjects and 5 patients with disseminated neoplasia were also studied.

The stimulation ratio of tritiated leucine incorporation in cultures of patients with glioma is significantly depressed, as in those with disseminated neoplasia, but not in patients with benign intracranial tumours. This impairment of cell-mediated immunity may have important implications for management of patients with intracranial tumour.

PHA concentration (μg/ml)	Normal subjects ($n = 49$)	Benign intracranial tumour ($n = 8$)	Glioma ($n = 9$)	Disseminated neoplasia ($n = 5$)
0·26	1·40 ± 0·04	1·33 ± 0·07 NS	1·21 ± 0·09 NS	0·94 ± 0·03 $P<0·01$
1·04	1·79 ± 0·06	1·62 ± 0·09 NS	1·42 ± 0·11 $P<0·05$	0·98 ± 0·06 $P<0·01$
2·08	2·00 ± 0·07	1·72 ± 0·12 NS	1·52 ± 0·13 $P<0·01$	1·00 ± 0·09 $P<0·001$
8·33	2·10 ± 0·07	1·83 ± 0·14 NS	1·45 ± 0·12 $P<0·001$	1·09 ± 0·11 $P<0·001$

All the results given as the mean stimulation ratio ± s.e.m. *P* value on *t*-test. NS, Not significant.

PAULY J. L., SOKAL J. E. and TIN HAN (1973) Whole-blood culture technique for functional studies of lymphocyte reactivity to mitogens, antigens and homologous lymphocytes. *J. Lab. Clin. Med.* **82**, 500–512.

WAHLSTRÖM T., LINDER E., SAKSELA E. and WESTERMARK B. (1974) Tumor-specific membrane antigens in established glial cell lines from gliomas. *Cancer* **34**, 274–279.

12. Changes induced in bile by female sex hormone

J. A. LYNN and L. F. WILLIAMS jun. (S. J. KARRAN), *Department of Surgery, Boston University Medical Center, Boston University School of Medicine, Boston, Mass.*

The increased incidence of gallstones in young women on the oral contraceptive pill suggests a role of female sex hormones in the formation of lithogenic bile. We studied the effect on hepatic bile flow and composition in 4 Rhesus monkeys with an intact enterohepatic circulation (Lynn et al., 1973) of oestrone and progesterone in daily doses of 0·01 and 0·1 mg/kg of body weight respectively for 7 days.

Oestrone produced a 26·2 per cent mean reduction in bile volume ($P<0·01$). Bile salt secretion fell from a mean of 6·680 to 5·520 mmol/24 hours ($P<0·05$). Cholesterol secretion increased from a mean of 0·115 to 0·225 mmol/24 hours ($P<0·05$). Phospholipid secretion fell from a mean of 0·980 to 0·897 mmol/24 hours ($P>0·1$, not significant). The mean bile salt pool fell from 1·33 mmol to 1·05 ($P<0·02$). The lithogenic index of hepatic bile increased from a mean of 0·38 to 1·2 ($P<0·005$). Progesterone caused no significant change in bile flow or composition ($P>0·1$). Oestrone produced bile supersaturated with cholesterol because of increased cholesterol secretion associated with decreased bile salt secretion due to a diminished bile salt pool.

These studies suggest that the production of lithogenic bile by oral contraceptives is due primarily to their oestrogen content.

LYNN J. A., WILLIAMS L., O'BRIEN J., WITTENBERG J. and EGDAHL R. H. (1973) Effects of estrogens upon bile: implications with respect to gallstone formation. *Ann. Surg.* **178**, 514–522.

13. Low dose heparin prophylaxis against fatal pulmonary embolism

V. V. KAKKAR and T. P. CORRIGAN, *Department of Surgery, King's College Hospital Medical School, London*

Several controlled trials have shown that low dose heparin is effective in reducing the incidence of deep vein thrombosis without increasing the risk of bleeding. However, its effectiveness in preventing fatal pulmonary embolism has yet to be determined, and therefore a multicentre trial was organized in which 31 centres took part. Patients over the age of 40 undergoing only major elective abdominal, thoracic or orthopaedic surgery were included. They were randomly allocated to a control or heparin group and, for each patient entered in the trial, essential information was recorded on a pro forma designed for computer analysis. The incidence of fatal pulmonary embolism was determined by autopsy examination. Altogether 4121 patients were admitted to the trial, 2076 in the control group and 2045 in the heparin group. Sixteen patients in the control group died of acute massive pulmonary embolism which was confirmed at autopsy, but only 2 in the heparin group. The difference is statistically significant (*P* < 0·01). There was no evidence of excessive blood loss during or after surgery.

Low dose heparin prophylaxis can now be recommended as the method of choice for preventing postoperative fatal pulmonary embolism.

14. A simple test for screening surgical patients likely to develop postoperative venous thrombo-embolism

S. SAGAR, D. P. THOMAS and V. V. KAKKAR, *Department of Surgery, King's College Hospital Medical School, London*

A simple and rapid test which could be used preoperatively to select patients who are likely to develop venous thromboembolic complications following surgery would be of great help in deciding which patients require 'active' prophylaxis. During blood clotting, thrombin is produced from its precursor, prothrombin, by the action of activated Factor X in the presence of a lipid and calcium ions. Thrombin thus formed initiates the development of a fibrin clot. Yin and Wessler (1969) have demonstrated the presence of a naturally occurring inhibitor of activated Factor X (XaI) in human plasma.

Factor XaI levels were measured in 25 patients undergoing total hip replacement. Blood samples were taken, for determining Factor XaI levels, before, during and for 5 days after operation. ^{125}I-fibrinogen was used to detect the presence of deep vein thrombosis (DVT). Ten (40 per cent) of the 25 patients developed DVT and in these patients the mean preoperative level of Factor XaI was 73·5 ± 6·9 (s.e.m.) per cent. In the patients who did not develop DVT the mean preoperative level was 101·5 ± 4·3 per cent (*P* < 0·01).

Low levels of Factor XaI in the immediate preoperative period correlate well with the subsequent development of thrombosis in these patients.

YIN E. T. and WESSLER S. (1969) Evidence for a naturally-occurring plasma inhibitor of activated Factor X: its isolation and partial purification. *Thromb. Diath. Haemorrh.* **21**, 398–401.

15. The effect of subcutaneous heparin and operation on antithrombin-III

A. N. NICOLAIDES, I. GORDON-SMITH, F. ZUBAIRI, R. BOWERS and R. C. G. RUSSELL, *Surgical Unit, St Mary's Hospital, London*

Small doses of heparin may prevent deep vein thrombosis by potentiating antithrombin-III (A-III), an inhibitor of activated Factor X (Yin and Wessler, 1970). A-III is consumed during clotting. We have determined the effect of operation and heparin on the blood levels of antithrombin-III.

Fifty patients undergoing general surgical operations were randomly allocated into a test group or a control group. The former received 5000 u. of subcutaneous heparin 2 hours before operation and 12-hourly for 8 days; the latter received subcutaneous saline. Plasma levels of A-III and of heparin were estimated before operation, 2, 4 and 6 hours after the subcutaneous injection on the day of operation and thereafter on the first, third and sixth postoperative days immediately before the morning injection.

In the control group A-III (mean preoperative level 28·54 ± 4·48 mg/100 ml) decreased progressively during and after operation; the reduction was statistically significant on the third postoperative day (25·49 ± 4·80 mg/100 ml; paired *t*-test, *P* < 0·025). The fall of A-III was faster in the heparin group (preoperative level 29·59 ± 4·43 mg/100 ml); significance was reached at 4 hours (26·03) ± 5·01 mg/100 ml; *P* < 0·0125). At 6 hours the fall of A-III in the test group was three times greater than the fall in the control group. There was no relation between plasma levels of heparin and the changes in A-III.

The results suggest that postoperatively heparin causes more A-III to be utilized.

YIN E. T. and WESSLER S. (1970) Heparin-accelerated inhibition of activated Factor X by its natural inhibitor. *Biochem. Biophys. Acta* **201**, 387–390.

16. Reversed segments after massive intestinal resection. Is transit delay hormone-mediated?

A. A. B. BARROS D'SA, T. L. KENNEDY, T. G. PARKS and K. D. BUCHANAN, *Departments of Surgery and Medicine, Queen's University and Royal Victoria Hospital, Belfast*

Hypermotility and rapid transit time are distinctive features of massive intestinal resection. In previous communications to the Surgical Research Society we showed that 75 per cent distal intestinal resection in dogs caused accelerated mouth to caecum transit which was slowed by reversal of the terminal 10 cm of the remnant (*P* < 0·001). We also demonstrated that after such resections plasma gastrin levels rose and levels of total glucagon-like immunoreactivity (GLI) fell (*P* < 0·05). It was suggested that these hormonal alterations were relevant to the mechanisms producing rapid transit.

In this study basal and stimulated levels of several circulating gastro-intestinal hormones were investigated after 75 per cent resection and 10-cm segmental reversal. Radio-immunoassay techniques were employed to measure gastrin, secretin, insulin, pancreatic glucagon and total GLI.

Gastrin levels were significantly lower in this group than in unoperated animals (*P* < 0·001) or after massive resection without reversal (*P* < 0·001). Total GLI levels in the reversal group were significantly higher than those after resection alone (*P* < 0·005).

Thus, resection was associated with accelerated transit, raised gastrin and lowered total GLI levels. Conversely, resection with reversal produced delayed transit, low gastrin and normal total GLI levels.

It is suggested that mechanical stasis produced by reversed segments after massive intestinal resection provokes specific humoral changes which mediate in delayed transit.

17. Respiratory function after oesophageal resection

J. BLACK, G. J. KALLOOR and J. LEIGH COLLIS, *Queen Elizabeth Hospital, Birmingham*

Respiratory function has been studied in 32 patients having oesophageal resection to compare the effects of two standard surgical approaches: 18 patients had a left thoracolaparotomy and 14 a laparotomy and separate right thoracotomy. The groups were similar in age, sex, chest symptoms and smoking habits. The double incision group were transfused slightly less blood but the operation took on average 8 minutes longer.

Arterial P_{O_2} was determined preoperatively and on the first and third postoperative days. Spirometry was done preoperatively and on the thirteenth postoperative day.

Preoperatively there was no significant difference between the groups in these parameters. On the first postoperative day both groups showed a pronounced fall in arterial P_{O_2} with a partial recovery on the third day. This recovery was greater in the double incision group and the difference was significant ($t = 2{\cdot}6$, $P < 0{\cdot}02$). Vital capacity and 1-second expiratory volume were reduced on the thirteenth day in both groups but without significant difference between the groups.

It is concluded that the double incision laparotomy and right thoracotomy approach affects respiratory function less than left thoracolaparotomy. When technically feasible it may be preferable in patients with respiratory impairment.

18. Action of a sterculia bulk-forming agent and smooth muscle relaxant versus bran in diverticular disease

G. SRIVASTAVA, A. N. SMITH and N. PAINTER, *Department of Clinical Surgery, University of Edinburgh and Manor House Hospital, London*

Cereal fibre has effects which are advantageous in diverticular disease: it lowers the colonic intraluminal pressure response to food and to prostigmine (Kirwan et al., 1974). In contrast, the sterculia bulk-forming agent Normacol given for 1 month to 10 patients with diverticular disease increased the pressure in the colon most significantly (motility index $+304 \pm 102{\cdot}5$, $P < 0{\cdot}01$) in response to food. The rise in pressure may follow precipitate movements of colon contents into the sigmoid colon after eating. The reduction in intestinal transit was from 90 to 70 hours (not significant), whereas after bran the reduction was to less than 40 hours ($P < 0{\cdot}01$). When Normacol was combined with a smooth muscle relaxant (alverine citrate), the basal, food-elicited and prostigmine pressures fell sharply (food $276 \pm 101{\cdot}5$; prostigmine 1209 ± 266), i.e. to the same levels as follow the consumption of bran (Kirwan et al., 1974).

The sterculia bulk former Normacol was as effective as bran in relieving 'painful' diverticular disease in a scored randomized clinical trial only if the smooth muscle relaxant was added (the bulk-forming agent alone relieved only the associated constipation). It is postulated that part of the mode of action of bran may be to relax the smooth muscle of the gut, since its actions compare more favourably with sterculia plus a smooth muscle relaxant than with a sterculia preparation alone.

KIRWAN W. O., SMITH A. N., MCCONNELL A. A., MITCHELL W. D. and EASTWOOD M. A. (1974) Action of different bran preparations on colonic function. *Br. Med. J.* **4**, 187–189.

19. A model for studying auto-allergy induced by cryosurgery

A. J. COOPER, J. D. FRASER and JANET IRVINE, *Surgical Division, Southampton University Medical School*

Cryosurgical remnants are potentially immunogenic. Whether such responses can be harnessed for therapeutic ends or whether they may constitute a threat of auto-allergy was investigated by examining the immunological status of guinea-pigs following cryosurgical treatment of one thymic lobe.

At 2–4 weeks after surgery animals were skin tested with 10^6 bone marrow cells, thymocytes and leukaemic (L2C) B lymphocytes. Reactions were read at 24 hours; serum and lymphoid cell suspensions were then prepared from them for *in vitro* cytotoxic assays, and their spleen weight indices were measured. Alternatively, syngeneic guinea-pigs were challenged with L2C tumour immediately after surgery.

Partial cryothymectomy caused significant splenomegaly against all of three control regimens, and reduced the median survival time following challenge with L2C tumour. Skin reactions were positive with thymocytes (6 mm mean diameter), bone marrow cells (9 mm) and L2C cells (10 mm) against a background of < 2 mm normal lymphocyte transfer reaction in control groups. However, ^{51}Cr release assays for cell- and antibody-mediated lysis of thymocytes and L2C cells were negative (< 2 per cent specific release) in all the groups.

These results demonstrate altered immunological responsiveness following cryosurgery which extend beyond reactivity against thymocyte-specific antigens.

20. The effect of surgery on the resistance of guinea-pigs to a transplantable tumour: a possible immunological explanation

A. R. TURNBULL, A. J. COOPER and JANET IRVINE (J. D. FRASER), *Surgical Division, Southampton University Medical School*

An animal model previously described (Cooper et al., 1974) has been used to study the effect of cholecystectomy on the survival of guinea-pigs after injection of a lethal dose of L2C leukaemic cells.

Surgery 6 days before the injection of tumour prolonged the mean survival time by 77 per cent ($P < 0{\cdot}01$) relative to that of the controls. Surgery 1 day after the tumour dose did not significantly affect the survival, but surgery 9 days after the tumour injection shortened the survival time by 35 per cent ($P < 0{\cdot}01$) compared with that of the control animals.

The possibility that this is an immunological phenomenon has been investigated. *In vitro* assays demonstrate at least two cytotoxic mechanisms which may promote or retard tumour growth. Comparative studies investigating the secondary response after challenge with sheep red blood cells show a similar variation. Surgery 7 days before challenge showed a response similar to that of the controls, but for 3 days before challenge the response was increased by 45 per cent. Surgery on the same day reduced the response by 59 per cent ($P < 0{\cdot}01$), and surgery 7 days after by 70 per cent ($P < 0{\cdot}01$).

In the clinical situation impairment of immunological responsiveness following surgery in cancer patients could alter the tumour–host relationship and enhance malignant growth potential.

COOPER A. J., IRVINE J. M. and TURNBULL A. R. (1974) Depression of immunological responses due to surgery. *Immunology* **27**, 393–399.

21. Acquired unresponsiveness to a Gross virus-induced lymphoma in W/Fu rats: evidence for both cellular and humoral suppressor mechanisms

J. A. MYBURGH and N. A. MITCHISON (D. J. DU PLESSIS), *Department of Surgery, University of the Witwatersrand Medical School, Johannesburg, and ICRF Tumour Immunology Unit, University College London*

The purpose of this study was the assessment of induction of tolerance to a highly immunogenic syngeneic Gross virus-induced lymphoma (C58NT)D in W/Fu rats, and an examination of the mechanisms involved in the production of specific unresponsiveness.

Rats were inoculated intraperitoneally within 24 hours of birth with the virus in the form of AKR mouse thymocytes and challenged subcutaneously with tumour 5 weeks later. In contrast to rats challenged primarily at 5 weeks (Shellam, 1974), these animals showed progressive tumour growth and failed to mount an appropriate *in vitro* cell-mediated immune response (CMI) to the tumour. In adoptive transfer experiments to sublethally irradiated (800 rad) syngeneic recipients, spleen cells from these 'tolerant' rats produced enhanced progressive tumour growth, and also abrogated the host protective effect of admixed tumour immune cells. This suppressor effect of 'tolerant' cells was abolished by prior irradiation (2000 rad) of the cells. *In vitro* studies with a ^{51}Cr-release lymphocytotoxicity assay showed similar effects. Suppressor effects *in vitro* were abolished by trypsinization of the cells. A blocking humoral factor, apparently active at target cell level, was also demonstrated in both *in vitro* and *in vivo* assays. It is concluded that acquired tolerance to an immunogenic virus-induced tumour in W/Fu rats can be produced by neonatal exposure to the virus, and that active mechanisms, involving both suppressor cells and humoral factors, are responsible for this state of acquired immunological unresponsiveness to the tumours.

SHELLAM G. R. (1974) Studies of a Gross virus-induced lymphoma in the rat. I. The cell-mediated immune response. *Int. J. Cancer* **14**, 65–82.

22. Comparison of fructose and glucose clearance during and after major surgery in man

D. O'B. MCCARTHY, P. D. WRIGHT and I. D. A. JOHNSTON, *Department of Surgery, University of Newcastle upon Tyne*

Fasting blood glucose is elevated and the rate of disappearance of infused glucose is reduced after major injury (Wright et al., 1974. Increased insulin antagonism is considered to play a part in post-traumatic glucose intolerance. Fructose metabolism is partly independent of insulin, but there is little information on the effect of injury on the metabolism of fructose by the body.

A study was planned to compare glucose and fructose clearance in two groups of 6 carefully matched male patients who had no metabolic diseases before and after major vascular surgical operations of the same severity. Fructose or glucose (25 g) was given intravenously over a 2-minute period before, during and at intervals for 8 days after surgery.

The rate of clearance of fructose was increased significantly during operation ($P<0{\cdot}01$), but had returned to preoperative levels by the first postoperative day. Glucose clearance, in contrast, was reduced during and throughout the 8 days of the study.

The fructose load produced a brisk insulin response before operation. This response was diminished and delayed during surgery. These findings suggest that fructose might be utilized as a calorie source more efficiently than glucose during and immediately after surgical operation.

WRIGHT P. D., HENDERSON K. and JOHNSTON I. D. A. (1974) Glucose utilization and insulin secretion during surgery in man. *Br. J. Surg.* **61**, 5–8.

23. The modification of the adaptive response to stress by carbohydrate-containing infusions

B. J. ROWLANDS, A. E. B. GIDDINGS and R. G. CLARK, *University Surgical Unit, Northern General Hospital, Sheffield, and Royal Devon and Exeter Hospital, Wonford, Exeter*

Insulin resistance is associated with simultaneous elevations of glucose and non-esterified fatty acids (NEFA) to satisfy postoperative energy requirements (Giddings, 1974). These changes may be modified by carbohydrate and amino acid infusions.

Basal plasma values±s.e.m. in 34 patients studied were as follows:

	Preoperative	Postoperative	*P* value
Glucose (mmol/l)	5·14±0·118	6·60±0·191	<0·001
NEFA (μmol/l)	103·1±5·11	119·6<4·31	<0·005

In 18 patients a 2-hour infusion of glucose, fructose or sorbitol (0·5 g/kg of body weight h^{-1}) produced significant falls in NEFA ($P<0{\cdot}001$, $<0{\cdot}005$ and $<0{\cdot}01$ respectively). Postoperatively these changes were associated with hyperglycaemia ($P<0{\cdot}005$) and rises in immunoreactive insulin ($P<0{\cdot}001$). Similar changes were observed in 4 patients receiving a 5-hour infusion of fructose and in 6 patients receiving a 2-hour infusion of L-amino acid 70 g/l and fructose 100 g/l.

Six patients received a provocative arginine infusion test (12 mg/kg of body weight min^{-1}). Preoperatively there was elevation of plasma glucose ($P<0{\cdot}001$) and a fall in NEFA ($P<0{\cdot}01$). Postoperatively there was no change in glucose and an insignificant fall in NEFA. The insulin response was similar in each test.

Infusions which contain carbohydrate alter the adaptive response to stress by reducing NEFA, but arginine maintains high levels of both NEFA and glucose. Amino acid infusions alone may thus have advantages over conventional nutritional regimens in stress situations.

GIDDINGS A. E. B. (1974) The control of plasma glucose in the surgical patient. *Br. J. Surg.* **61**, 787–792.

24. Comparison of highly selective vagotomy (HSV) plus dilatation and of vagotomy with a drainage procedure (V+D) in the treatment of pyloric stenosis secondary to duodenal ulceration

M. J. MCMAHON, M. J. GREENALL, D. JOHNSTON and J. C. GOLIGHER, *University Department of Surgery, The General Infirmary, Leeds*

The hypothesis that patients with pyloric stenosis would obtain better clinical results after HSV plus dilatation of the stenosis than after V+D (Johnston et al., 1973) was tested by 'blind' review of two groups of patients at a follow-up clinic: 23 consecutive patients who had undergone HSV for pyloric stenosis were compared with a series of 23 patients treated by V+D for pyloric stenosis by another surgeon. The length of follow-up was the same (0–4 years) and the two groups were similar with respect to age, sex, weight, maximum acid output and length of ulcer history.

	HSV	V+D
Operative mortality	0	0
Reoperation for stasis	2	1
Recurrent ulceration	0	0
Perfect result (Visick grade 1)	75%	45%
Good result (Visick grades 1+2)	95%	75%
Early dumping	10%	10%
Diarrhoea	5%	20%
Vomiting	10%	14%
Flatulence	10%	23%
Epigastric fullness	15%	32%

The results demonstrate the remarkable propulsive powers of the hypertrophied gastric antrum in pyloric stenosis: re-stenosis occurred in only 2 patients after HSV who did well after gastric drainage. Patients had a much better chance of obtaining a perfect result, without side effects, after HSV than after V+D. These findings support the hypothesis, which should be tested further in a prospective random trial.

JOHNSTON D., LYNDON P. J., SMITH R. B. and HUMPHREY C. S. (1973) Highly selective vagotomy without a drainage procedure in the treatment of haemorrhage, perforation, and pyloric stenosis due to peptic ulcer. *Br. J. Surg.* **60**, 790–797.

25. Multivariate analysis of clinical and operative findings associated with biliary sepsis

M. R. B. KEIGHLEY, A. R. CRAPP, R. FLINN and J. ALEXANDER-WILLIAMS, *The General Hospital, Birmingham*

Operations for biliary disease are associated with a high incidence of wound sepsis (Report, 1960) and septicaemia, particularly in jaundiced patients (Flemma et al., 1967). Biliary micro-organisms are responsible for these complications, and prophylactic antibiotics will minimize this morbidity (Bevan and Williams, 1971). Effective prophylaxis depends upon satisfactory tissue antibiotic concentrations at the time of bacterial contamination (Burke, 1961).

To identify patients with biliary micro-organisms and hence avoid indiscrimant use of prophylactic antibiotics, a multifactorial analysis of clinical and operative findings has been obtained from a prospective study of patients requiring biliary surgery; none had been given preoperative antibiotics ($n=181$).

Cluster analysis of 17 preoperative and 11 operative variables defined a high risk ($n=45$) and a low risk ($n=136$) population, where the incidence of biliary sepsis was 67 and 15 per cent respectively ($P<0{\cdot}001$). Seven findings were much more common in the high risk than in the low risk group ($P<0{\cdot}001$). These 'high risk factors' were: jaundice at operation, recent rigors, emergency surgery, age over 70 years, previous biliary surgery, common duct obstruction and stones in the bile duct. In 57 patients where one or more of these 'factors' was present the bile was infected in 34 (60 per cent). When

4 'high risk factors' occurred in the same patient (20 cases) biliary organisms were isolated in 19 (95 per cent).

We conclude that the presence of one or more 'high risk factors' indicates a group in whom prophylactic chemotherapy would be advised.

BEVAN P. G. and WILLIAMS J. D. (1971) Rifamide in acute cholecystitis and biliary surgery. *Br. Med. J.* **3**, 284–287.

BURKE J. F. (1961) The effective period of preventive antibiotic action in experimental incisions and dormal lesions. *Surgery* **50**, 161–168.

FLEMMA R. J., FLINT L. M., OSTERHOUT S. and SHINGLETON W. E. (1967) Bacteriological studies of biliary tract infection. *Ann. Surg.* **166**, 563–572.

REPORT (1960) Public Health Laboratory Service Report. *Lancet* **2**, 659–663.

26. The effect of noxytiolin (Noxyflex) in peritonitis due to perforated appendicitis

D. W. KING, J. F. GURRY, R. B. ELLIS-PEGLER and B. N. BROOKE, *Department of Surgery, St George's Hospital Medical School, London*

The evidence for the value of noxytiolin in peritonitis is contradictory. Intraperitoneal injection of noxytiolin has been shown to offer significant protection against a lethal Gram-negative peritonitis in guinea-pigs, and these results have been thought to account in part for a low mortality rate in a series of patients with faecal peritonitis (Browne and Stoller, 1970). Other workers were unable to show that lavage with noxytiolin was more beneficial than with Hartmann's solution in faecal peritonitis in rats (Cleaver et al., 1970).

A rabbit model of perforated appendicitis similar pathologically and bacteriologically to the condition in humans has been used in a controlled trial of peritoneal instillation of noxytiolin. There was a 17·6 per cent mortality in the control group and 55·6 per cent mortality in the trial group ($P<0{\cdot}05$). A greater postoperative weight loss was seen in the trial group compared with that of the controls ($P<0{\cdot}01$).

In a double blind clinical trial of 27 patients with perforated appendicitis there was no significant difference in wound infection rate, length of stay in hospital or other complications between a placebo control group and a group treated with intraperitoneal noxytiolin solution at the time of operation.

BROWNE M. K. and STOLLER J. L. (1970) Intraperitoneal noxytiolin in faecal peritonitis. *Br. J. Surg.* **57**, 525–529.

CLEAVER C. L. T., HOPKINS A. D., KEE KWONG K. C. NG and RAFTERY A. T. (1974) The effect of postoperative peritoneal lavage on survival, peritoneal wound healing and adhesion formation following faecal peritonitis: an experimental study in the rat. *Br. J. Surg.* **61**, 601–604.

27. Collagen metabolism in infected colonic anastomoses

T. T. IRVIN, *University Department of Surgery, Royal Infirmary, Sheffield*

It is alleged that colonic anastomoses fail in the presence of infection due to increased tissue collagenolysis (Hawley, 1973). However, there have been no detailed studies of collagen metabolism in infected anastomoses.

Twenty-five male Sprague–Dawley rats were labelled with 5-^{3}H-L-proline for 6 weeks before collagen metabolism was studied in normal and infected anastomoses in the left colon. The anastomoses were removed 3 or 7 days after surgery, and the hydroxyproline content and radioactivity (DPM) in the salt-soluble (SSC), acid-soluble and insoluble (ISC) collagen fractions were measured (Prockop et al., 1961).

Anastomoses on days 3 and 7 were compared with control values in anastomoses removed from the same animals on the day of surgery. On day 3 there was a 23–25 per cent reduction in ISC, and a 30 per cent reduction in DPM of ISC in normal and infected anastomoses. SSC in normal anastomoses increased by 82 per cent, but there was a 32 per cent reduction in infected anastomoses (Wilcoxon test, $P<0{\cdot}01$). Similar differences in DPM were found in SSC ($P<0{\cdot}005$). On day 7 the size of all the collagen fractions was increased, and there was a small increase in DPM. There was no significant difference between normal and infected anastomoses.

The results are compatible with the thesis that infection causes increased collagenolysis, but they could also be explained by a reduction in colonic collagen synthesis.

HAWLEY P. R. (1973) Causes and prevention of colonic anastomotic breakdown. *Dis. Colon Rectum* **16**, 272–277.

PROCKOP D. J., UDENFRIEND S. and LINDSTEDT S. A. (1961) A simple technique for measuring the specific activity of labelled hydroxyproline in biological materials. *J. Biol. Chem.* **236**, 1395–1398.

28. Effects of gastric surgery on differential emptying of solid and liquid components of the gastric contents

R. C. HEADING, P. TOTHILL, G. P. MCLOUGHLIN and D. J. C. SHEARMAN (D. C. CARTER), *Gastrointestinal Section, Department of Therapeutics and Department of Medical Physics, University of Edinburgh*

Following a natural meal the solid and liquid components of the gastric contents are believed to empty through the pylorus at different rates (Hunt and Knox, 1968). Using a scintiscanning method with double isotope labelling of a meal (Heading et al., 1974), we have studied the effects of gastric surgery on emptying rates of the two components. Measurements were performed during the period 35–120 minutes after ingestion of a meal, so that emptying involving mechanisms particular to the early phase was excluded.

In 18 control patients given a meal of cornflakes, sugar and milk the solid marker emptied more slowly than the liquid marker ($P<0{\cdot}01$). In 19 patients with duodenal ulcer, 13 patients with highly selective vagotomy and 14 with truncal vagotomy and pyloroplasty (Heineke-Mikulicz) mean emptying rates of both markers were slower than in the controls, but the relationship between them was maintained. However, in 6 patients with Billroth II gastrectomy solid emptying was faster, though liquid emptying was slower than in the controls, the relationship being significantly altered ($P<0{\cdot}01$).

The results suggest that differential emptying of the solid and liquid components of the gastric contents is effected by the gastric antrum, is largely independent of the actual emptying rate and is unaltered by pyloroplasty.

HEADING R. C., TOTHILL P., MCLOUGHLIN G. P. and SHEARMAN D. J. C. (1974) Gastric emptying rate measurement in man: a double isotope scanning technique for simultaneous study of solid and liquid phases. (Abstr.) *Gut* **15**, 841.

HUNT J. H. and KNOX M. T. (1968) Regulations of gastric emptying. In: *Handbook of Physiology*, Section 6. *Alimentary Canal*. Washington DC, American Physiological Society.

29. The effect of carbenoxolone and phenol red on the permeability of steroid-treated gastric mucosa, using ^{99}Tc as a tracer

B. M. NEWMAN, J. B. ELDER and I. E. GILLESPIE, *University Department of Surgery, Royal Infirmary, Manchester*

Carbenoxolone and phenol red are known to alter gastric mucosal function. The effects of these substances alone and in combination with prednisolone on the gastric mucosa of 64 rabbits, using ^{99}Tc as a tracer, have been studied on mucosal flaps using an *in vivo* chamber.

Oral carbenoxolone 15 mg and 50 mg daily for 7 days caused a significant decrease in flux of ^{99}Tc from the lumen in both the antrum ($P<0{\cdot}001$) and the fundus ($P<0{\cdot}001$). When 1 ml of a solution of phenol red (25 mg/l) was placed on the mucosa a similar decrease in flux was noted ($P<0{\cdot}001$).

Prednisolone 10 mg daily for 7 days increased the antral but not the fundic flux of ^{99}Tc. This selective antral effect was significantly reduced by combining 50 mg/day carbenoxolone with prednisolone over the period of study. The addition of phenol red to the chamber in steroid-treated animals decreased the mucosal ^{99}Tc flux significantly below control values ($P<0{\cdot}001$).

This work suggests that carbenoxolone and phenol red may have a 'protective' effect on steroid-treated gastric mucosa.

30. The effect of portal and systemic venous drainage of the pancreas on glucose and insulin metabolism

J. COLLIN, R. M. R. TAYLOR and I. D. A. JOHNSTON, *Department of Surgery, University of Newcastle upon Tyne*

Persistent hyperinsulinaemia and hypoglycaemia have been reported (Lillehei et al., 1970) after heterotopic pancreatic transplantation and has been attributed to diversion of pancreatic vein blood from the portal vein (Sells et al., 1972). Experiments were designed to examine this hypothesis.

Group I comprised 8 dogs in which all pancreatic tissue was excised other than the pancreatic tail which continued to drain into the portal vein. Intravenous glucose tolerance tests revealed normal glucose clearance on the first postoperative day with an increased insulin response (mean 60·9 μu./ml, $P<0{\cdot}05$), while on the fourth and twenty-second postoperative days glucose clearance was reduced ($P<0{\cdot}005$) and the insulin response was diminished (mean 14 μu./ml, $P<0{\cdot}05$).

In group II, 14 totally pancreatectomized dogs had a heterotopically autotransplanted pancreatic tail, the venous drainage being to the iliac veins. Fasting hyperinsulinaemia was present on the second postoperative day ($P<0{\cdot}025$), but hypoglycaemia did not occur. The insulin response to glucose was increased on the first postoperative day (mean 69·4 μu./ml, $P<0{\cdot}025$) but decreased subsequently (mean 20·9 μu./ml, $P<0{\cdot}05$). Glucose clearance was normal on the first postoperative day, but was subsequently decreased on the twenty-second postoperative day ($P<0{\cdot}05$). Comparisons of glucose clearance, insulin response, fasting insulin and glucose levels revealed no significant differences between the groups.

It is concluded that there is no demonstrable advantage to glucose homeostasis from portal as opposed to systemic venous drainage of the pancreas.

LILLEHEI R. C., SIMMONS R. L. and NAJARIAN J. S. (1970) Pancreatico-duodenal allotransplantation. *Ann. Surg.* **172**, 405–436.

SELLS R. A., CALNE R. Y., HADJIYANAKIS V. and MARSHALL V. C. (1972) Glucose and insulin metabolism after pancreatic transplantation. *Br. Med. J.* 3, 678–681.

31. Changes in volume of the breast during the menstrual cycle

T. HAMILTON and MARY E. RANKIN, *Department of Clinical Surgery, University of Edinburgh*

Perhaps the difficulty in achieving reproducible measurements accounts for the paucity of information on the nature of changes in breast volume which, as every women appreciates, takes place during the menstrual cycle. A simple apparatus has been devised by which the volume of both breasts can be measured by their immersion in water through a rectangular orifice in a plywood board placed over a suitable container. The displaced water is collected via a side channel conduit. By accurately replacing sites of contact at both inframammary sulci, shoulders and sternal notch, reproducibility to within ±6 per cent has been obtained.

Daily measurements have been done together with daily temperature recordings and weekly oestrogen and progesterone levels to determine the time of ovulation. In normal women volume increases of between 30 and 40 per cent have been obtained, the increase beginning at ovulation, reaching a peak 24–48 hours before the onset of menstruation and returning to the baseline by the end of menstruation. Studies to assess the possible effects of the contraceptive pill are in progress.

32. Synthesis of oestradiol by human breast cancer

W. R. MILLER and A. P. M. FORREST, *Department of Clinical Surgery, University of Edinburgh*

Thirteen human breast cancers have been studied with regard to their ability to synthesize oestradiol-17β from the C19 steroid testosterone. Slices of each tumour were incubated *in vitro* with 7α(^{3}H)-testosterone for 2 hours at 37 °C.

The conversion of testosterone to oestradiol-17β was determined by measuring the incorporation of the radioactive label into oestradiol after purification by thin layer chromatography and characterization by chemical derivative formation. Simultaneous estimates were carried out to characterize C19 steroid metabolites.

All the tumours metabolized significant amounts of testosterone (20–50 per cent), and in 6 unequivocal evidence for the synthesis of significant amounts of oestradiol was obtained. In 2 tumours conversions were 0·22 and 0·37 per cent, but in 4 smaller amounts (0·04–0·07 per cent) were produced.

As previously described with other breast tumours (Miller et al., 1973), all the tumours metabolized testosterone to Δ4-androstenedione, 5α-dihydrotestosterone and 5α-androstanediol.

The synthesis at tumour level of active oestrogen from precursor C19 (androgenic) steroids may be of prime importance in determining the nature of hormone dependence.

MILLER W. R., MCDONALD D., FORREST A. P. M. and SHIVAS A. A. (1973) Metabolism of androgens by human breast tissue. *Lancet* **1**, 912–913.

33. Clinical correlates of cell-mediated reactivity to autologous tumour antigens in breast cancer

A. R. TURNBULL and B. M. JONES (J. D. FRASER), *Surgical Division, Southampton University Medical School, and Tenovus Research Laboratories, Velindre Hospital, Cardiff*

The leucocyte migration inhibition test (Søborg and Bendixen, 1967), an *in vitro* test of cell-mediated immunity, has been performed serially on patients with breast cancer. The patients form part of an on-going clinical trial comparing simple mastectomy alone with simple mastectomy plus radical radiotherapy for operable breast cancer (clinical stages I and II). An axillary lymph node biopsy was routinely performed at operation.

At 2 months there was a significant difference in reactivity between lymph node positive (11 out of 38) and lymph node negative patients (3 out of 37; $P=0{\cdot}05$). Comparison between the observed and irradiated groups at 6 months showed that 8 out of 24 (33 per cent) of the treated patients were positive but none of the 18 patients in the watched group reacted ($P=0{\cdot}05$). At 7 days, 2 months and 12 months there was no significant difference between these groups.

No significant correlation could be demonstrated between reactivity in the leucocyte migration test and reactivity *in vivo* as shown by histological examination of the tumours and lymph nodes and by skin testing.

These results suggest that residual tumour might maintain sensitivity after removal of the primary antigenic stimulus. Similarly, irradiation may cause disruption of nodal metastases with release of circulating antigenic fragments which produce positive reactions apparent at 6 months.

SØBORG M. and BENDIXEN G. (1967) Human lymphocyte migration as a parameter of hypersensitivity. *Acta Med. Scand.* **181**, 247–256.

34. The immune reaction to human breast cancer tissue

M. MAUREEN ROBERTS and ELEANOR M. BASS, *Department of Clinical Surgery, University of Edinburgh*

A study is in progress to determine the incidence of immune reactivity in patients with primary breast cancer towards their own tumours, and to correlate the findings with clinical prognosis.

Extracts of autologous tumours standardized for protein content have been used throughout in tests of both cellular and humoral immunity with the following results:

1. Cellular immunity: Strong positive reactions to tumour extract were observed in 7 of 37 patients by skin testing and in 11 of 40 patients by the leucocyte migration inhibition test; serum blocking factors were found in only 7·5 per cent.

2. Humoral immunity: Serum antibodies to tumour were found in 4 of 60 patients tested by Ouchterlony analysis and 2 of 40 patients by the complement fixation test; serum IgA was raised and the relative levels of immunoglobulins in breast cancer tissue were altered compared with those in normal breast tissue, with high levels of IgM in some and abnormal IgG in others when estimated by immunodiffusion and demonstrated by immunofluorescent techniques.

We conclude that by the methods used approximately 20 per cent of patients at the time of mastectomy have a strong cellular immune reaction to their own tumours. The incidence of circulating antibodies is low, but interesting abnormalities may exist at tissue level.

35. The leucocyte migration inhibition test in cancer immunology

P. R. ARMITSTEAD, G. GOWLAND and G. R. GILES, *University Department of Surgery, St James's Hospital, and University Department of Immunology, The General Infirmary, Leeds*

The leucocyte migration test is used as a test of cell-mediated immunity against cancer. However, the test lacks sensitivity and produces results which are difficult to interpret.

We have attempted to explain some of the inconsistencies by using the separated mononuclear and granulocyte fractions in 10 per cent homologous AB serum or 10 per cent autologous serum and a colorectal tumour antigen. Normal patterns of migration for each cell fraction were established in homologous AB serum of 6 control subjects. In autologous serum the mononuclear cell fraction migrated normally with tumour antigen, but 3 out of 6 of the tests using the granulocyte fraction and non-separated leucocytes showed apparent migration inhibition.

Nine patients with colorectal cancer were examined. Five showed migration inhibition using non-separated leucocytes in both sera. Significant migration inhibition occurred in all the tests with the mononuclear cell fraction in AB serum. Using the granulocyte fraction, migration inhibition was not seen with AB serum, though two tests were positive in autologous serum.

The study shows increased sensitivity of the migration inhibition tests using a mononuclear cell fraction, and that autologous serum may interfere directly with migration of granulocytes, by an action not dependent upon the release of inhibitory factors from sensitized lymphocytes.

36. Plasma esterolytic activity during acute pancreatitis in the human

A. CUSCHIERI and KAREN J. WORTHINGTON, *Department of Surgery, University of Liverpool*

There has been a renewed interest in the administration of aprotinin (Trasylol) in acute pancreatitis since the favourable report on its use by Trapnell et al. (1974). In the present study plasma esterolytic activity was measured serially in 12 patients with acute pancreatitis, 10 patients with intra-abdominal inflammatory conditions (contrast group) and 7 healthy volunteers. The esterolytic activity was assayed in samples of heparinized plasma using benzoyl arginine ethyl ester with the modified NAD/alcohol dehydrogenase method (Worthington and Cuschieri, 1974). The serum amylase was also measured in patients with acute pancreatitis. *In vitro* inhibition of plasma esterolytic activity was studied using Trasylol, ovomucoid and soybean inhibitor. The results are presented as means ± s.d.

The plasma esterolytic activity in the contrast group was 617·0 ± 385·0 mu./100 ml and this did not differ from the value in the control of 611·0 ± 275·0 mu./100 ml ($P = 0{\cdot}98$). The level of esterolytic activity in acute pancreatitis varied with the duration of the disease:

Duration of pancreatitis (d)	Esterolytic activity (mu./100 ml)	Serum amylase (Somogyi units/100 ml)
0–2	2270 ± 859*	2759 ± 1848
2–4	1755 ± 946*	637 ± 425
4–6	863 ± 409	259 ± 224
6–8	1261 ± 675*	116 ± 20
>8	1235 ± 575*	204 ± 90

* Significant difference from controls ($P < 0{\cdot}01$) using the Wilcoxon rank test.

An 82 ± 24 per cent inhibition was obtained when Trasylol (0·2 ml, 2000 Kallikrein inactivator units) was added to 0·3 ml of plasma from patients with acute pancreatitis. Soybean inhibitor gave a 51 ± 29 per cent inhibition and ovomucoid 34 ± 28 per cent.

It is concluded that a sustained esterolytic activity reflecting the release of proteolytic enzymes occurs in acute pancreatitis. The activity is maximal during the first 4 days of the illness, with a later rise between the sixth and the tenth days. Although Trasylol inhibits this activity, the dose required would need to be much higher than that which has been used clinically.

TRAPNELL J. E., RIGBY C. C., TALBOT C. H. and DUNCAN E. H. L. (1974) A controlled trial of Trasylol in the treatment of acute pancreatitis. *Br. J. Surg.* **61**, 177–182.

WORTHINGTON K. J. and CUSCHIERI A. (1974) A study on the kinetics of pancreatic kallikrein. *Clin. Chim. Acta* **52**, 129–136.

37. *In vitro* studies on human renal pelvis muscle

N. LONGRIGG (I. E. GILLESPIE), *University Department of Surgery, The Royal Infirmary, Manchester*

The possible role of autonomic nerves in modifying motor activity of the human renal pelvis is as yet unknown.

Isolated strips (10 preparations) of human renal pelvis, obtained at operation, were studied in an organ bath by an isometric technique. Platinum electrodes positioned alongside the tissue provided electrical transmural stimulation.

Preparations responded to adrenaline, noradrenaline and phenylephrine by an increase in tension. This response could be abolished by pretreatment with small doses of phentolamine (160 ng/ml), suggesting that it was mediated by α-adrenoceptors. A similar excitatory response to the addition of acetylcholine could be antagonized by atropine in a concentration of 20 ng/ml, indicating the presence of muscarinic receptors.

An increase in tension after electrical stimulation occurred only when the pulse width was greater than 4 msec (current strength 150 mA, frequency 2–32 Hz). By comparison with other autonomically innervated tissues, such a large pulse width suggests that in renal pelvis muscle the response was *not* caused by nerve depolarization, and most probably represented direct muscle stimulation. This was confirmed by finding that exactly similar qualitative and quantitative responses were obtained before and after treatment of the tissues with tetrodotoxin, a potent neurotoxin which selectively blocks nerve as opposed to muscle depolarization.

These results suggest that the receptor sites identified are not effectively innervated, and that motility of the human renal pelvis is completely independent of the autonomic nervous system.

38. Effective temporary hepatic support in acute liver failure

M. SLAPAK and D. C. WILKINS, *Department of Surgery, University of Cambridge*

A new canine model of acute liver failure has been developed (Slapak and Wilkins, 1975). The purpose of this study was to determine the length of support time needed for otherwise lethal liver damage to recover.

Twelve dogs (group A) had a 2-hour ischaemic interval imposed on two-thirds of their liver (main lobe, ML); the remaining third (supporting lobe, SL) served to decompress the portal circulation and hepatically support the animal. At the end of this period the afferent blood supply to the ischaemic ML was allowed to resume whilst that to the SL was permanently arrested. All 12 dogs temporarily recovered and were ambulant. Coma and death due to ischaemic liver necrosis took place 22 ± 3 hours after resumption of flow. Clinical, biochemical and EEG evidence of acute liver failure as the cause of death was present.

In group B (10 dogs) the blood supply to the ML was normal but the SL was permanently ligated. All the animals survived in good health until sacrifice 3 weeks later. No evidence of liver abnormality was present.

In group C (7 dogs) a 2-hour ischaemic period was imposed on the ML as in group A, but the blood supply to the SL was not arrested. All 7 dogs survived until 10–14 days when the SL was resected. Six of the dogs survived in good health for a further 1 month till sacrifice. At 12 hours after release mean SGPT was 1700 i.u., prothrombin time 24 seconds and BSP retention 24 per cent. These values became normal within 3 days. Delta waves in the EEG also recovered. Histologically, evidence of a recovering pericentral vein necrosis was seen. The study shows that effective liver support for 10–14 days completely reverses an otherwise 100 per cent lethal hepatic injury.

SLAPAK M. and WILKINS D. C. (1975) A new canine model of acute liver failure without a portacaval shunt. *Tenth Congress European Society for Experimental Surgery, Paris*, 1975.

39. Effect of superimposed cold ischaemia on a long warm ischaemic interval

S. ROGERS and M. SLAPAK, *Department of Surgery, University of Cambridge*

Although the mean warm ischaemic interval of cadaveric kidneys transplanted by us in 1974 (62 minutes) has not altered from that in 1968 (64 minutes), the mean cold ischaemic interval has trebled. A study to define the possible accumulative effect of varying cold superimposed on warm anoxia was therefore performed in two groups of rats.

In group A, 35 diuresing kidneys were removed and 45 minutes' ischaemia at 37 °C imposed. Seven kidneys in each of subgroups I–V of group A were then rapidly cooled and stored at 4 °C for 0, 6, 12, 18 and 24 hours respectively. At these times the kidneys were removed and the ability of 0·3-mm slices to take up PAH ^{125}I from a buffer solution was determined—the S : M ratio (Lannon et al., 1971). This was $3{\cdot}1\pm1{\cdot}3$, $2{\cdot}7\pm0{\cdot}4$, $2{\cdot}9\pm0{\cdot}2$, $1{\cdot}9\pm0{\cdot}3$ and $1{\cdot}5\pm0{\cdot}3$ respectively. Values at 0, 6 and 12 hours differed ($P<0{\cdot}001$) from those at 18 and 24 hours. In the control group B warm ischaemia was not imposed. In subgroup VI (12 kidneys) 24 hours' cold ischaemia only was imposed (S : M ratio $2{\cdot}9\pm0{\cdot}4$). In subgroup VII (14 kidneys) no ischaemia of any sort was imposed (S : M ratio $7{\cdot}3\pm0{\cdot}9$).

It has previously been shown (Slapak and Rogers, 1975) that a kidney S : M ratio of less than 2 carried a 25 per cent risk of uraemic death even after a 3-week support period ensured by a delayed contralateral nephrectomy. The data therefore show that, under the experimental conditions imposed, a cold ischaemic interval of longer than 12 hours has a significantly detrimental effect on kidneys already exposed to a 45-minute warm ischaemic interval. Nevertheless, such periods of cold or warm ischaemia alone are well tolerated.

LANNON S. G., DOSSETOR J. and BICKIS I. (1971) Viability testing of kidneys for transplantation. *Invest. Urol.* **9**, 180–183.

SLAPAK M. and ROGERS S. (1975) An evaluation of two predictive tests of eventual kidney function. *Transplant. Proc.* **7**, 110–112.

40. The immunosuppressive effect of surgery and its relation to rejection in the immediate postoperative period

R. F. M. WOOD, P. R. F. BELL, AILEEN C. GRAY and S. G. PACKER, *Department of Surgery, University of Leicester, and Department of Pathology, University of Glasgow*

Surgery is known to cause a temporary depression of the immune response (Bancewicz et al., 1973). This study was undertaken to assess the effect of a strong antigenic challenge with an allograft upon this reaction.

Cell-mediated immunity was studied using the leucocyte migration test before and after surgery in two groups of 6 dogs with either autotransplants (group 1) or allotransplants (group 2). The autotransplanted animals were sensitized with *Bordetella pertussis* before surgery and this agent was used to assess their immune response. In the allograft group reactivity was measured in response to donor liver, spleen, lymph node and kidney. In both groups blast cell activity was monitored by the spontaneous uptake of ^{14}C-labelled thymidine by lymphocytes. The blood urea, serum creatinine and immunological tests were performed daily after operation.

In group 1 cell-mediated immunity was impaired for 3 days and then returned to normal. Blast cell activity (^{14}C-labelled thymidine) was, however, impaired for several weeks, showing a small but temporary rise on day 5. In group 2 cell-mediated immunity was increased by the sixth day with significant inhibition of migration. Blast cell activity (^{14}C-labelled thymidine) was again reduced after surgery, and there was a temporary increase between the sixth and ninth postoperative days.

These results suggest that spontaneous blast cell transformation as a non-specific measure of immune activity was depressed after both auto- and allotransplants. However, cell-mediated immunity to a specific antigen is only temporarily affected by operation and the development of sensitization to transplantation antigens occurs despite the fall in blast cell activity.

BANCEWICZ J., GRAY A. C. and LINDOP G. (1973) The immuno suppressive effect of surgery—a possible mechanism. *Br. J. Surg.* **60**, 314–315.

41. Prognostic significance of circulating inhibitory factors of mixed lymphocyte culture for human renal allograft survival

D. E. OSBORN and J. E. CASTRO, *Urology and Transplant Unit, Royal Postgraduate Medical School, London*

Survival of human renal allografts may be influenced by circulating humoral factors. Patients who underwent cadaver renal transplantations were examined for factors which inhibit mixed lymphocyte culture (MLC), and the results were correlated with graft survival.

Inhibition of MLC was measured in a one way culture by adding 20 per cent of test serum and the results compared with culture containing control AB serum. In each experiment 6 combinations of recipient and unrelated mismatched lymphocytes were studied. Significant inhibition occurred if the ratio of transformation in control and test cultures was at least 2·5.

In the patients with a successful transplant serum taken before operation caused blocking of MLC in 2 of 6 patients and in only 4 of 36 lymphocyte combinations. Serum taken after transplantation caused blocking in 4 of 7 patients and only 4 of 42 combinations.

In patients whose transplanted kidney was rejected, blocking occurred before transplantation in all the patients and in 20 of 36 lymphocyte combinations. Serum taken after transplantation caused blocking in 7 of 8 patients and in 21 of 42 combinations. Four kidneys were removed for non-immunological causes.

These observations suggest that the presence of circulating inhibitory factors of MLC are associated with a significantly increased incidence of transplant rejection.

42. Rat cardiac allograft survival by treatment with promethazine-HCl

S. W. JAMIESON (J. D. LEWIS), *Northwick Park Hospital, Harrow, Middlesex*

In rat cardiac allografts the production of humoral antibody is associated with progressive and irreversible intimal thickening. This process is seen in human transplants and is the main barrier to long term survival of cardiac and renal grafts.

Electron micrographic studies performed on cardiac xenografts between guinea-pigs and rats show that massive intravascular coagulation of platelets and fibrin occurs in response to antibody insult. The graft vascular endothelium is destroyed subsequent to platelet contraction.

Promethazine-HCl (Phenergan) inhibits antibody production (Gusdon et al., 1972) and the second stage of platelet aggregation (Mills and Roberts, 1967). In a control series of 24 cardiac allografts between AgB,AgC compatible rats, 12 were rejected before 20 days (mean rejection time 15 days). Ten showed spontaneous survival, probably as a result of enhancing antibody on the endothelium. Ninety transplants were performed in recipients treated with promethazine-HCl. Continuous treatment resulted in survival of all the grafts and reduction of intimal thickening. Cessation of treatment on day 4 after transplantation had no effect, but treatment continued to day 8 only again produced total survival.

It is suggested that endothelial cell integrity is important for the survival of transplants, because it both reduces lymphocytic infiltration of the graft and subsequent intimal thickening. Promethazine-HCl has the effect of protecting the endothelium from antibody-induced platelet damage when antibody begins to circulate.

GUSDON J. P., MOORE V. L., MYRVIK Q. N. and HOLYFIELD P. A. (1972) Promethazine hydrochloride as an immunosuppressant. *J. Immunol.* **108**, 1340–1344.

MILLS D. C. B. and ROBERTS G. C. K. (1967) Membrane active drugs and the aggregation of human blood platelets. *Nature (Lond.)* **213**, 35–38.

43. Experimental revascularization of myocardial infarction

J. N. FABIANI, A. DELOCHE, J. P. CAMILLIERI, D. JOSEPH, M. SCHLUMBERGER, J. RELLAND and A. CARPENTIER, *Laboratoire d'Etudes des Greffes et Prothèses Cardiaques, Institut Biomédical des Cordeliers, Paris*

Histo-enzymatic studies of the myocardium and electron microscopic study of the capillary network have been carried out in order to evaluate the effect of early revascularization of myocardial infarction in the rat.

The histo-enzymatic study was carried out in 56 animals. In 14 the left coronary artery was ligated, creating an extensive transmural anterolateral infarct within the first hour with disappearance of phosphorylase activity at the end of 6 hours; a marginal necrotic zone was identified by succinyl dehydrogenase, the activity of which ceased after 48 hours. In 42 animals ligation of the left coronary artery was temporary, lasting 1 hour (27 cases), 6 hours (12 cases) and 12 hours (3 cases). Enzymatic studies demonstrated a reduction, by half of the size of the infarct, mainly in the marginal zone; this occurred in 75 per cent of the cases when the ligature was released after 1 hour and in 50 per cent of the cases when the ligature was released at the end of 6 hours.

Study of the capillary circulation during infarction was undertaken in 60 animals by measuring coronary perfusion pressure and by performing electron microscopy after the injection of indian ink. Coronary perfusion pressure was found to be significantly increased in ischaemias lasting more than 20 minutes. Electron microscopic study revealed a marked pyknosis of the endothelial cells as well as interstitial oedema, reducing the calibre of the capillaries and favouring sludging of erythrocytes.

We conclude that: (1) histo-enzymatic study permits a more precise mapping of the infarcted area and further documents the reversibility of myocardial infarction following early revascularization; (2) reversibility of infarction is found mainly in the marginal zone of ischaemia and is inconstant; (3) endothelial and subendothelial changes are secondary factors leading to capillary blockage aggravating the primary ischaemic lesion.

44. Interpretation of lower oesophageal pressure measurements

C. PEREZ-AVILA and T. T. IRVIN, *Department of Surgery, Royal Infirmary, Sheffield*

It is claimed that manometric measurements of lower oesophageal sphincter pressure (LESP) provide useful information in the diagnosis of gastro-oesophageal reflux (Ingelfinger, 1971). However, little is known of the day-to-day variation in LESP and the accuracy of such measurements has been questioned (Stef et al., 1974).

The reproducibility of pressure measurements in the lower oesophagus has been studied in patients without symptoms of gastro-oesophageal reflux. Using a water-perfused triple catheter assembly, mean and end-expiratory LESP and gastric and oesophageal pressures were measured, twice on the same day in 26 subjects, and once on separate days in 11 subjects. The pressure response to abdominal compression was recorded and the stomach/oesophageal sphincter pressure gradient or barrier pressure (BP) was calculated.

Sequential measurements on the same day gave reproducible results for LESP ($r = 0{\cdot}89$) and BP ($r = 0{\cdot}91$), and the response of the BP to abdominal compression was also reproducible ($r = 0{\cdot}89$). Studies on different days showed significant variations in LESP ($r = 0{\cdot}37$) and BP ($r = 0{\cdot}13$).

The results suggest that there is a significant day-to-day variation in the tone of the lower oesophageal sphincter, and that manometric studies of the gastro-oesophageal junction should be interpreted with caution.

INGELFINGER F. J. (1971) The sphincter that is a sphinx. *New Engl. J. Med.* **284**, 1095–1096.

STEF J. J., DODDS W. J., HOGAN W. J., LINEHAN J. H. and STEWART E. T. (1974) Intraluminal esophageal manometry: an analysis of variables affecting recording fidelity of peristaltic pressures. *Gastroenterology* **67**, 221–230.

45. A simple clinical method for measurement of gastric emptying of solid meals

D. G. OSTICK, G. GREEN, K. HOWE, I. W. DYMOCK and D. J. COWLEY, *Departments of Surgery and Medicine, University Hospital of South Manchester, and Department of Biophysics, University of Manchester*

The radio-isotope technique used for the measurement of gastric emptying of solid meals in man requires complex and expensive scintiscanners (Griffiths et al., 1968) or gamma cameras (Jones et al., 1970), which are only available in a few centres. We have evaluated a simpler technique which utilizes a single scintillation detector and have compared the results obtained with those from a gamma camera.

Twenty healthy volunteers ate a standard meal labelled with 500 μCi of ^{99}Tc sulphur colloid. Radioactivity from the stomach was counted simultaneously with (1) a gamma camera with an on-line computer (Hancock et al., 1974) and (2) a single scintillation detector positioned over the area of maximal activity. All the subjects were studied standing.

In each of the 20 subjects the rate of emptying as measured by the two methods correlated closely (mean $r = 0{\cdot}95$, range 0·77–0·99). The mean percentage of activity which remained in the stomach at any time interval after eating was virtually identical for the two techniques. The mean half emptying time ($T_{\frac{1}{2}}$) with the gamma camera was $49{\cdot}3 \pm 19{\cdot}8$ (s.d.) min and with the scintillation detector $48{\cdot}2 \pm 21{\cdot}1$ min.

The single scintillation detector provides a reliable and inexpensive method. It could be used as a simple quantitative test of gastric emptying in patients with gastric disorders.

GRIFFITHS G. H., OWEN G. M., CAMPBELL H. and SHIELDS R. (1968) Gastric emptying in health and gastroduodenal disease. *Gastroenterology* **54**, 1–7.

HANCOCK B. D., BOWEN-JONES E., DIXON R., DYMOCK I. W. and COWLEY D. J. (1974) The effect of Metoclopramide on gastric emptying of solid meals. *Gut* **15**, 462–467.

JONES T., CLARK J. C., KOCAK N., COX A. G. and GLASS H. I. (1970) Measurement of gastric emptying using the scintillation camera and ^{129}Cs. *Br. J. Radiol.* **43**, 537–541.

46. Plasma gastrin after proximal gastric vagotomy and vagotomy and antrectomy

C. M. S. ROYSTON, W. M. COOKE, R. C. G. RUSSELL, S. R. BLOOM and J. SPENCER, *Departments of Surgery and Endocrinology, Royal Postgraduate Medical School, and Surgical Unit, St Mary's Hospital, London*

The effect of proximal gastric vagotomy (PGV) on plasma gastrin is still uncertain; conflicting results have been reported and different techniques used. We have used a standardized insulin-bicarbonate test (Cowley et al., 1973) to study gastrin release before and 10 days and 3 months after operation in 9 patients undergoing PGV and in 12 undergoing vagotomy and antrectomy (TVA). The two groups were comparable as regards basal gastrins ($33\pm4{\cdot}3$ and $33\pm4{\cdot}9$ pg/ml respectively) and insulin-stimulated rise in gastrin ($32\pm7{\cdot}6$, $29\pm6{\cdot}2$ pg/ml) before operation.

After PGV mean basal gastrins doubled at 3 months ($67\pm22{\cdot}2$ pg/ml). Insulin-stimulated release fell at 10 days but was back to preoperative values at 3 months. After TVA basal gastrins were unchanged at 10 days and 3 months. Stimulated gastrin release fell to half the preoperative value ($16\pm3{\cdot}8$ pg/ml at 10 days, $14{\cdot}6\pm5{\cdot}2$ pg/ml at 3 months).

Rise in basal gastrin after PGV has been related to fall in acid secretion. However, in our preoperative subjects basal acid output was positively correlated with basal gastrin ($P<0{\cdot}001$), although insulin-stimulated gastrin release was negatively correlated with peak acid output to pentagastrin ($P<0{\cdot}01$).

Our findings differ from those of others, who found either unchanged basal gastrin after PGV (Clark et al., 1973) or a fall in basal gastrin after antrectomy (McGuigan and Trudeau, 1972).

CLARK C. G., LEWIS M. R., STAGG B. H. and WYLLIE J. H. (1973) Effect of proximal gastric vagotomy on gastric acid secretion and plasma gastrin. *Gut* 14, 293–299.

COWLEY D. J., BARON J. H., HANSKY J. and KORMAN N. G. (1973) The effect of insulin hypoglycaemia on serum gastrin and gastric acid in normal subjects and patients with duodenal ulcer. *Br. J. Surg.* 60, 438–443.

MCGUIGAN J. E. and TRUDEAU W. L. (1972) Serum gastrin levels before and after vagotomy and pyloroplasty or vagotomy and antrectomy. *New Engl. J. Med.* 286, 184–188.

47. Diurnal rhythm of gastrin and glucagon

B. W. ELLIS, R. C. G. RUSSELL, S. R. BLOOM and H. A. F. DUDLEY, *Surgical Unit, St Mary's Hospital, London*

A number of hormones involved in intermediary metabolism (e.g. growth hormone) have been shown to have a diurnal rhythm and specific secretion during various sleep stages (Pawel et al., 1972). However, there are no detailed studies of these aspects of the gastro-intestinal hormones; we have studied glucagon and gastrin in 6 healthy volunteers to determine whether there is either a diurnal rhythm or relationship to sleep stage.

Five volunteers had blood samples taken at 20-minute intervals over 24 hours and 1 volunteer had samples taken at 5-minute intervals overnight. All the subjects ate standard meals. Sleep was determined from electro-encephalogram, electro-oculogram and skin resistance recordings.

Glucagon levels showed marked fluctuation both on 20- and 5-minute sampling. Thus, the oscillation frequency of this hormone is likely to be less than 5 minutes. The levels were increased by food. The mean basal gastrin was 15 pg/ml. The rate of change of gastrin levels was slower than that of glucagon, and the oscillation frequency is probably at least 20 minutes. There was no apparent diurnal variation or association with sleep stage of either of these hormones.

It is concluded that the stages of sleep play no part in the control of these hormones and that studies of them can be undertaken without sleep recording. Meaningful data of glucagon levels would involve sampling at least every 2 minutes, whereas gastrin need not be sampled more often than every 20 minutes.

PAWEL M. A., SASSIN J. F. and WEITZMAN E. D. (1972) The temporal relationship between HGH release and sleep stage changes at nocturnal sleep onset in man. *Life Sci.* 11, 587–593.

48. Effect of growth hormone release inhibitory hormone on gastric secretion in the cat

J. D. REED, MARGITTA ALBINUS, A. GOMEZ-PAN, R. HALL, M. H. THOMPSON, C. W. VENABLES, G. M. BESSER and A. V. SHALLY, *Departments of Physiology, Medicine and Surgery, University of Newcastle upon Tyne, St Bartholomew's Hospital, London, and VA Administration Hospital and Tulane University School of Medicine, New Orleans, Louisiana*

Growth hormone release inhibitory hormone (GH-RIH) has been shown to have a direct inhibitory effect on the gastric acid and pepsin secretory response to pentagastrin, and on the acid secretory response to food (Gomez-Pan et al., 1975). We have further investigated the effect of GH-RIH on intact and vagotomized gastric fistula cats.

An infusion of 10 μg/kg h^{-1} of GH-RIH inhibited by about 90 per cent, gastric acid secretion stimulated by 6·0 μg/kg pentagastrin subcutaneously, and 8 μg/kg h^{-1} given by intravenous infusion similarly inhibited the response to insulin 0·2 μ/kg intravenously. In contrast, the same GH-RIH infusion failed to inhibit the secretory response to 100 μg/kg h^{-1} of histamine (as base).

The results show that GH-RIH inhibits the response to all the stimuli we have studied except histamine, again raising the possibility that histamine is the final common mediator in gastric acid secretion.

GOMEZ-PAN A., REED J. D., ALBINUS M., SHAW B., HALL R., BESSER G. M., COY D. H., KASTIN A. J. and SCHALLY A. V. (1975) Direct inhibition of gastric acid and pepsin secretion by growth-hormone release-inhibiting hormone (Somatostatin) in cats. *Lancet* 1, 888–890.

49. Intraluminal oxygen in acute ischaemia of the small intestine

K. SHUTE (A. MARSTON), *Department of Surgery, Royal Postgraduate Medical School, London*

The mortality in acute ischaemia of the small intestine in man is over 90 per cent regardless of treatment. This experiment demonstrates the use of intraluminal oxygen in this condition in the rat.

Two comparable groups of 18 rats were anaesthetized with methoxyfluothane in oxygen. The superior mesenteric artery was clamped for 2 hours, then released, with immediate restoration of mesenteric circulation in all the animals. No treatment was given to the control group. In the treated group after 30 minutes' arterial occlusion 20 ml of gaseous oxygen were injected transmurally into the lumen of the small intestine. After release of the clamp, the mortality in each group was compared after 48 hours. Autopsies were carried out at death or after sacrifice at 48 hours.

Two rats in the control group (11 per cent) and 11 of those treated (61 per cent) survived for 48 hours. Statistical analysis showed this difference to be significant at the 1 per cent level ($P<0{\cdot}01$). All the animals dying before 48 hours had necrotic bowel filled with blood, whilst the survivors, sacrificed at 48 hours after occlusion, had viable bowel with macroscopically normal circulation.

Thus, intraluminal oxygen produced a statistically significant increase in survival in rats subjected to acute small intestinal ischaemia.

50. Effect of the histamine H_2 receptor antagonist, cimetidine, on insulin-induced gastric secretion in man

D. C. CARTER, R. LOGAN, J. A. H. FORREST, I. ANSELL, R. C. HEADING and D. J. C. SHEARMAN, *Department of Clinical Surgery and Gastrointestinal Section, Department of Therapeutics, Edinburgh University*

The histamine H_2 receptor antagonist metiamide is a potent inhibitor of gastric secretion in man (Carter et al., 1974; Milton-Thompson et al., 1974) but limited by bone marrow toxicity. Cimetidine is a new antagonist which does not appear to have toxicity problems.

Paired tests were carried out in 6 healthy volunteers. Insulin was infused for 150 minutes in a dose of 0·03 u./kg h^{-1}, and between 60 and 135 minutes 100 mg/h of cimetidine were infused. Saline replaced cimetidine in control studies. Volume, acid concentration and acid output were lower during cimetidine infusion, the acid output during the last 60 minutes of cimetidine being 4·36 ± 3·87 mmol/h compared with 17·73 ± 7·58 mmol/h in control tests (mean ± s.d. of mean; $P < 0{\cdot}001$). Pepsin output was not significantly affected by cimetidine. Plasma gastrin rose to a mean value of 57·8 ± 21·0 (s.e.m.) pg/ml after 150 minutes of cimetidine, compared with 40·4 ± 9·3 pg/ml in control tests ($P < 0{\cdot}15$).

Cimetidine is therefore a potent inhibitor of insulin-induced acid secretion in man, but this effect does not extend to pepsin secretion. If this compound remains free from toxicity it may have potential in the treatment of the peptic ulcer diathesis.

CARTER D. C., FORREST J. A. H., WERNER M., HEADING R. C., PARK J. and SHEARMAN D. J. C. (1974) Effect of histamine H_2-receptor blockade on vagally induced gastric secretion in man. *Br. Med. J.* 3, 554–556.

MILTON-THOMPSON G. J., WILLIAMS J. G., JENKINS D. J. A. and MISIEWICZ J. J. (1974) Inhibition of nocturnal acid secretion in duodenal ulcer by one oral dose of metiamide. *Lancet* **1**, 693–694.

51. Value of perioperative acid tests in predicting recurrent ulceration after vagotomy

J. M. HOOD, E. F. ANNE SPENCER, K. D. MACRAE and T. KENNEDY, *Royal Victoria Hospital, Belfast*

In predicting recurrent ulcer after vagotomy, Kronborg (1974) found early postoperative insulin tests valueless, but preoperative acid output after pentagastrin correlated well with recurrence rates.

We have re-examined the value of preoperative pentagastrin test meals and postoperative insulin tests. In this series 274 prospectively studied patients have been followed up for 2–9 years after vagotomy of various types and 16 recurrent ulcers have been found, i.e. 5·8 per cent recurrence.

Preoperatively the mean basal acid in patients without recurrence was 4·2 mEq/h compared with 8·7 mEq/h in those with recurrence ($P < 0{\cdot}001$). With basal acid under 2 mEq/h the recurrence rate was 1·4 per cent compared with 18·5 per cent in those with more than 10 mEq/h. After pentagastrin stimulation there was no correlation between recurrence and either the peak or maximum output. Insulin tests showed a mean basal acid of 1·8 mEq in the patients with recurrence and 0·8 mEq in the remainder ($P < 0{\cdot}05$). Peak, maximum and total output were all significantly higher in those with recurrence ($P < 0{\cdot}001$). Strict Hollander criteria were positive in 24 patients, but only 5 of these developed recurrence.

These findings indicate that preoperative basal acid measurements and early postoperative basal and post-insulin levels all have predictive value.

KRONBORG O. (1974) Gastric acid secretion and risk of recurrence of duodenal ulcer within six to eight years after truncal vagotomy and drainage. *Gut* **15**, 714–719.

52. Angiotensin II and vasopressin in haemorrhagic shock

M. A. TEHRANI, B. STUART, A. REYES, G. MCGARRITY, I. MCA. LEDINGHAM and J. J. MORTON, *University Department of Surgery, and MRC Blood Pressure Unit, Western Infirmary, Glasgow*

The renin-angiotensin system may be involved in the pathogenesis of irreversible haemorrhagic shock (Jakschik et al., 1974). The elevation of angiotensin II (AII) associated with shock may be prevented by a converting enzyme inhibitor (SQ20881) with the effect of increasing long term survival in dogs (Errington and Rocha E Silva, 1974). In the present experiments the effect of SQ20881 on cardiovascular, and in particular myocardial, performance was examined in two groups of spontaneously breathing, anaesthetized dogs subjected to haemorrhagic shock. Mean arterial blood pressure was reduced to 35–40 mm Hg and maintained for either 1·5 or 2 hours before retransfusion. In one of the two groups SQ20881 was given before and at an early stage of the shock. A third group of unbled dogs was also studied. Plasma AII, vasopressin and, when appropriate, AI were measured by a radio-immunoassay method.

In the group of 10 dogs not given SQ20881 plasma AII rose by 37 times during shock. During retransfusion 5 animals died of acute cardiac failure, and of the 5 survivors, only 2 had relatively normal left ventricular function.

In the group of 5 dogs given SQ20881 the plasma AII only doubled. All survived with relatively normal left ventricular function.

Plasma vasopressin was grossly elevated in both groups.

JAKSCHIK B. A., MARSHALL G. R., KOURIK J. L. and NEEDLEMAN P. (1974) Profile of circulating vasoactive substances in haemorrhagic shock and their pharmacologic manipulation. *J. Clin. Invest.* **54**, 842–852.

ERRINGTON M. L. and ROCHA E SILVA M. jun. (1974) On the role of vasopressin and angiotensin in the development of irreversible haemorrhagic shock. *J. Physiol.* (*Lond.*) **242**, 119–141.

53. Energy levels in splanchnic organs following severe haemorrhage and reinfusion

T. V. KEAVENY, S. K. CUNNINGHAM and P. FITZGERALD, *Department of Surgery, University College, Dublin*

The concentrations of ATP, ADP and AMP were determined in splanchnic organs in anaesthetized dogs subjected to severe haemorrhagic shock and reinfusion (Crowell et al., 1969). Three groups of 7 animals each were studied: untreated bled animals, bled animals pretreated with allopurinol 50 mg/kg and unbled controls. The concentrations of ATP 2 hours following reinfusion are reported below. The total ATP + ADP + AMP showed the same pattern.

Plasma levels of the lysosomal enzymes acid phosphatase and β-glucuronidase were determined as indicators of lysosomal damage, since released proteases from splanchnic lysosomes have been strongly implicated in the irreversibility of shock. Plasma acid phosphatase and β-glucuronidase rose to very high levels in the untreated shocked group but were significantly lower in the allopurinol pretreated group ($P < 0{\cdot}0005$ and $P < 0{\cdot}01$ respectively).

This study indicates that: (1) in untreated severely bled dogs the ATP concentrations in pancreas, liver and duodenum are not restored to normal 2 hours following reinfusion; (2) allopurinol pretreatment results in essentially normal ATP, ADP and AMP concentrations in these organs; (3) allopurinol pretreatment reduces the rise in plasma lysosomal enzymes.

	(1) Unbled controls	(2) Bled untreated	(3) Bled allopurinol-pretreated	Significance of (2) vs. (3) (*P*)
Pancreatic ATP	1·921 ± 0·26	0·898 ± 0·30	1·780 ± 0·34	< 0·0005
Liver ATP	1·195 ± 0·29	0·620 ± 0·17	1·192 ± 0·47	< 0·01
Duodenal ATP	1·804 ± 0·09	1·218 ± 0·42	1·874 ± 0·36	< 0·025
Splenic ATP	0·721 ± 0·28	0·571 ± 0·17	0·606 ± 0·05	NS

All the results given as the ± s.d. in μmol/g wet weight. NS, Not significant.

CROWELL T. W., JONES C. E. and SMITH F. E. (1969) Effect of allopurinol on haemorrhagic shock. *Am. J. Physiol.* **216**, 744–748.

54. Comparison of dextran 70 and hydroxyethyl starch in volume replacement

J. A. R. SMITH, J. N. NORMAN, A. SMITH and G. SMITH, *Department of Surgery, University of Aberdeen*

Both plasma and dextran solutions are commonly used for volume replacement in shock therapy but both have many disadvantages. Hydroxyethyl starch solution (HES) may have the advantages of dextran without its disadvantages, but its evaluation, particularly in shock, is incomplete. This study aims at comparing dextran 70 with HES in an established canine shock model.

Refractory shock was induced in 20 dogs by maintaining arterial pressure at 40 mm Hg by haemorrhage for 2 hours. At the end of this period the remaining shed blood was discarded and sufficient dextran or HES was infused to maintain central venous pressure at 2–4 mm Hg. Measurements of cardiac output, stroke volume, peripheral resistance and oxygen availability, consumption and debt were made at 15-minute intervals for 2 hours.

Both groups of dogs became progressively haemodiluted to a minimum haematocrit of 22 per cent of the resting value and both groups required similar volumes of fluid to maintain normovolaemia. Cardiac output, peripheral resistance and oxygen availability were similar in both groups, but tissue oxygen consumption was significantly greater in the groups given HES and the oxygen debt was repaid in this group. There was no evidence that haemodilution altered the course of shock and there was no significant difference in the dilution and expansion achieved by dextran 70 or HES. This suggests that HES is worthy of further consideration.

55. Effect of heparin and of acid-citrate-dextrose solution on screen filtration pressure of blood in experimental hypotension

B. J. PARDY and H. A. F. DUDLEY, *Surgical Unit, St Mary's Hospital Medical School, London*

Heparin is widely used to lessen the risk of microthrombosis in areas where perfusion is temporarily reduced and also appears to be effective when disseminated intravascular coagulation occurs as a consequence of generalized hypoperfusion. Nevertheless, in clinical practice isolated limbs do not always recover after restoration of their circulation, and experimentally heparin has not prevented microcirculatory obstruction in either the rat kidney (Diethelm and Wilson, 1971) or adrenal (Kovacs et al., 1966).

Screen filtration pressure (SFP) is a measure of microaggregation of blood; therefore, we have studied the effects of heparin and acid-citrate-dextrose (ACD) on SFP during and after haemorrhagic hypotension induced in 5 greyhounds by a bleed to a mean pressure of 90 mm Hg sustained for 3 hours and followed by reinfusion. SFP is expressed as the fourth root of the difference in pressure required to force saline at constant rate through a 20 μ filter before and after the passage of a standard amount of blood.

The results are tabulated and show that heparinized blood always causes more obstruction than does ACD blood; during and after shock the difference is greatly increased. Therefore, heparin may not be the ideal agent to protect the microcirculation during hypoperfusion.

	SFP			
	After induction	2 hours before shock	During shock	4 hours after shock
ACD blood	1·43±0·15	1·53±0·11	1·86±0·15	1·53±0·28
Heparinized blood	1·89±0·17	1·65±0·16	3·26±0·12	2·78±0·29

DIETHELM A. G. and WILSON S. J. (1971) Obstruction to the renal microcirculation after temporary ischaemia. *J. Surg. Res.* 11, 265–276.

KOVACS K., CARROLL R. and TAPP E. (1966) Temporary ischaemia of the rat adrenal gland. *J. Pathol.* 91, 235–240.

56. A new approach to thrombolytic therapy

V. V. KAKKAR and S. SAGAR, *Department of Surgery, King's College Hospital Medical School, London*

Several studies have now clearly shown that fibrinolytic therapy is highly effective in dissolving venous thrombi and pulmonary emboli. The most satisfactory method of streptokinase administration for producing maximum thrombolytic effect with the minimum hazard to the patient remains to be determined. In this paper we report the rationale and the preliminary results of a study where small doses of streptokinase were given intermittently in combination with plasminogen infusion to produce maximum thrombolytic effect.

In vitro studies were performed using 20 human thromboemboli removed at post-mortem. An initial perfusion with ^{131}I-labelled plasminogen showed an uptake by the thrombus about 3 times higher than that of the perfusion fluid. Subsequent perfusion with buffer containing streptokinase produced rapid and complete lysis. Twelve consecutive patients with extensive deep vein thrombosis confirmed by venography were divided into two groups: one group received 600 000 units of streptokinase every day for 5 days, and the other group 80–120 mg of plasminogen followed by 600 000 units of streptokinase, again for 5 days. No lysis of thrombi was observed in the group receiving streptokinase only, while 80 per cent of thrombi were completely lysed in those receiving streptokinase and plasminogen.

Our conclusions are that the new approach is safer, cheaper and much more effective than conventional thrombolytic therapy.

57. Coagulation and fibrinolytic responses during operative surgery

M. J. BUTLER, B. J. BRITTON, MURIEL SMITH, CHRISTINE HAWKEY and M. H. IRVING, *Departments of Surgery, St Bartholomew's Hospital, London, Hope Hospital, Salford, and the Nuffield Institute of Comparative Medicine, London Zoo*

Previous studies have demonstrated the changes in coagulation and fibrinolysis that follow operation but not the changes that occur during the operation itself. These changes have particular relevance as most postoperative venous thromboses are apparent within 48 hours and are thought to begin during operation.

Fourteen measurements of coagulation and fibrinolysis have been studied in 50 patients during elective abdominal surgery. Samples were taken immediately before operation, after induction of anaesthesia, halfway through the operation and at the end of operation.

Whole blood clotting time (WBCT), measured by thrombelastography, showed progressive shortening, this time at the end of the operation being significantly shorter than that of the preoperative sample ($P<0·001$).

No significant changes occurred in the activity of Factors II, V and X, but there was a highly significant rise in Factor VIII ($P<0·001$). This rise is unlikely to be of major significance in the shortening of WBCT as similar rises after exercise and venous occlusion are not accompanied by comparable WBCT changes.

Progressive activation of fibrinolysis began after the induction of anaesthesia, the changes being maximal by the midpoint of the operation ($P<0·005$), but tending to reverse by the end of the operation. Although there is no detectable difference between the coagulation and fibrinolytic responses of patients who develop deep vein thrombosis and those who do not, the marked hypercoagulability that develops during operation is likely to be a contributory factor in the development of venous thrombosis.

58. Nutritional skin blood flow before and after chemical sympathectomy

J. J. MORRICE, A. M. HARPER, D. W. SHORT, W. REID, J. K. WATT, J. POLLOCK and L. J. BLUMGART, *University Department of Surgery, Royal Infirmary, and Peripheral*

Vascular Unit, Royal Infirmary and Belvidere Hospital, Glasgow

The measurement of the clearance of ^{133}Xe from the skin is a reliable indication of capillary blood flow and therefore nutritional flow (Sejrsen, 1971).

We have used the epicutaneous ^{133}Xe technique (Sejrsen, 1968) to measure nutritional skin blood flow in the dorsum of the foot in normal controls and in patients with peripheral vascular disease before and after phenol injection of the lumbar sympathetic chain.

Under uniform resting conditions and at a constant room temperature (20 °C), ^{133}Xe clearance was measured with a scintillation detector, and the dermal nutritional flow calculated from the fast component of the resultant bi-exponential clearance curve. In 33 control patients (66 limbs) a mean value of $5{\cdot}2 \pm 1{\cdot}8$ (s.d.) ml/100 g tissue min^{-1} was obtained.

In a group of 33 patients with peripheral vascular disease skin blood flow before and after unilateral phenol block was measured. On the day following phenol injection a mean increase in skin flow of 71 per cent was obtained ($P < 0{\cdot}005$). At 1 month after injection the mean increase over the pre-injection flow was 51 per cent ($P < 0{\cdot}005$).

Simultaneous measurements of the skin flow in the non-sympathectomized limb showed no significant alteration in skin flow before and after injection at either 1 day or 1 month.

We conclude that phenol injection of the lumbar sympathetic chain effectively increases nutritional skin blood flow.

SEJRSEN P. (1968) Atraumatic local labelling of skin by inert gas: epicutaneous application of Xenon-133. *J. Appl. Physiol.* **24**, 570–572.

SEJRSEN P. (1971) Measurement of cutaneous blood flow by freely diffusible radioactive isotopes. MD Thesis, Copenhagen.

59. A blind clinical trial comparing ultrasound detection with established techniques to predict the site of incompetent perforating veins

K. G. BURNAND, T. F. O'DONNELL, M. LEA THOMAS and N. L. BROWSE, *St Thomas's Hospital, London*

Accuracy in excess of 80 per cent has been claimed (Miller et al., 1971) for ultrasound localization of incompetent perforating veins (ICPV) comparable to that previously reported for phlebography (Thomas et al., 1972). Unlike previous reports, this is a blind study which simultaneously compares three methods of ICPV detection with venous pressure profiles and operative findings.

ICPV localization on the medial side of 32 legs was made by clinical examination, ultrasound and ascending phlebography, each by a different observer. All the patients had pressure measurements made in a foot vein while standing at rest and during excercise. ICPVs were confirmed at operation (a long medial incision) by a positive bleed-back test.

The results of each test is expressed as a percentage of the surgical findings.

	Correct	False positive	False negative
Clinical	53	69	47
Phlebography	57	21	43
Ultrasound	67	113	33

The only significant difference in these results is that phlebography produces less false positives than ultrasound.

All the legs whose pressure drop on exercise was less than 40 per cent, in the presence of a thigh tourniquet, had ICPVs. If the foot vein pressure during exercise is abnormal we suggest that the only way to detect all the ICPVs is by using a full medial calf incision.

THOMAS M. L., MCALLISTER V., ROSE D. H. and TONGE K. (1972) A simplified technique of phlebography for the localisation of incompetent perforating veins of the legs. *Clin. Radiol.* **23**, 486–491.

MILLER S. S., GROSSMAN J. A. and FOOTE A. V. (1971) The ultrasonic detection of incompetent perforating veins. *Br. J. Surg.* **58**, 872.

Br. J. Surg. Vol. 62 (1975) 668–669

Obituary

Vincent Zachary Cope

KT, MD, MS, FRCS

1881–1974

ZACHARY COPE lived to the ripe old age of 93, but this was probably the least of his many varied achievements. Even in growing older, he never grew old, as was well evidenced by the publication of the fourteenth edition of the book for which he is most famous, *Early Diagnosis of the Acute Abdomen*, in 1972, less than 3 years before he died and 50 years after the first edition appeared in print. As an erstwhile dresser, registrar and colleague of his I am proud to possess a signed copy of this last edition—the signature clear and legible, the message above it lucid and warm.

Surely no surgical textbook has ever had the active life of this one. Generations of young surgeons all over the world have reason to be eternally grateful to him for its sound practical wisdom. In so many ways it reflects the character of its author, not only in its longevity but in its clarity of thought and expression, its basic common sense and its infallible appreciation of primary values.

Zachary Cope, the son of a north country Methodist minister, was a modest man with the quiet courtesy and manner of the Victorian era. But this apparently unhurried approach to life, of which he enjoyed to the full so many facets, hid a dynamic and intense personality which enabled him to cover, seemingly quite unruffled, a vast and varied field of interests in which he was all too often unseen and unheard and certainly to far too great an extent unsung.

In his youth qualification from St Mary's with honours in Surgery and Forensic Medicine in the London MBBS of 1905 was followed by the MD in 1907 and the MS and FRCS in 1909, and culminated in appointment to the St Mary's consultant staff in 1911. Man and boy he was an ardent protagonist of St Mary's and the hospital owes him much both in example and precept. In the First World War he served typically as a humble and hard-working RAMC captain in several theatres of war, was mentioned in dispatches and from the experience he gained in Mesopotamia produced his first venture into the world of medical literature—*Surgical Aspects of Dysentery*, published in 1921. Then in the period between the two World Wars came his time of fulfilment as a sound safe surgeon, as a gifted clinical diagnostician, as a highly successful and popular teacher and as an invaluable guide, counsellor and friend to a vast number of students, younger staff, colleagues and all sorts of medical institutions, associations and colleges. He was essentially a very human person—outgoing and warm-hearted. Though himself abstemious, the natural warmth of his personality embraced all those with whom he came into contact. He seemed to have an inexhaustible store of goodwill towards men—and it is very doubtful if he ever had a real enemy.

His students showed by deed their appreciation of his teaching as they flocked to his informatively instructive ward rounds; his patients trusted him implicitly—none more so than the children who came under his care, surely the indelible hallmark of a good doctor; and his juniors reacted automatically to his genuine, positive and continuing interest in them and their future. Who amongst those fortunate enough to have received them can have failed to be delighted by the amusing little outpourings of doggerel verse that arrived punctiliously every Christmas, or at times of recognized success.

To those who really knew him he showed a rather unexpected sense of quietly sardonic humour.

In this College his active service stretched over many valuable years; a full term Councillor and a Vice-President, a member of the Court of Examiners and a prolific giver of eponymous lectures. Few men can have equalled his record of four Hunterian, the Arris and Gale, the Vicary, the Tomes and the Bradshaw lectures!

His chief institutional interests outside the College lay principally with the BMA, on the Council of which he served for many years, ultimately becoming Vice-President and for which he chaired many committees, perhaps the most important being that on medical auxiliaries; and with the Medical Society of London of which he became President, Orator and the giver of its annual Lettsomian lecture. But he was also deeply involved in the affairs of the Royal Society of Medicine of which for many years he was Honorary Librarian and was very deservedly made an Honorary Fellow. He received a similar recognition from the Faculty of History of the Worshipful Society of Apothecaries, and in due course, most fittingly (and to the great delight of his host of friends), received the accolade of Knight Bachelor in the first Honours List of the Queen in the Coronation Year.

In the Second World War he held the post of Sector Medical Officer in the Emergency Medical Service and did yeoman work 'standing in' for many of his junior colleagues. Not surprisingly, this led to the very responsible task of chairing the National Medical Manpower Committee in the immediate post-war years.

At this stage he began to turn more to his second great love—that of literature. Zachary Cope was an erudite man, well and widely read, and undoubtedly had a natural flair for writing. At no time, however, did he lose his abiding interest in surgery and medicine and, though himself remaining essentially the humane and clinical exponent of the art, he had a lively appreciation of the dramatic and dynamic changes that science and technology were effecting in modern surgery. His writings were protean and prolific, and the results highly informative and easily readable. As examples, apart from his surgical books and articles, he wrote the *History of the Royal College of Surgeons of England* in 1959 and the *History of St Mary's Hospital Medical School* in its centenary year; he edited two volumes (clinical) of the *Medical History of the* 1939/45 *War*, and several biographies including those of Florence Nightingale, Cheselden and Aimroth Wright. All this, as one can see, amounted to a stupendous amount of work, but it was work that really gave him keen personal pleasure—he called it his 'self-indulgence'—and amazingly enough it still left him a modicum of time to develop his minor interests of music and, perhaps rather surprisingly, motoring, of which he was an early pioneer.

In his kaleidoscopic life Zachary Cope ensured for himself an enduring place in the history of surgery. His friends—and they were legion—will mourn his passing, but they will know their own lives are the richer for his having lived. His mind and his spirit remained unquenchable to the end—a man of many parts—a man small in stature but big in heart.

PORRITT

Br. J. Surg. Vol. 62 (1975) 670–672

Reviews and notices of books

A Textbook of Surgery

Edited by Mahadevan, Madras. 250×185 mm. Pp. 1167+xiv. Illustrated. 1974. Bombay: Asia Publishing House. 125R.

WITH the changing face of surgery the writing of a general textbook that is completely acceptable to all surgeons has become an impossibility. Mr Mahadevan is to be congratulated on his achievement in compiling this book, which is aimed primarily at meeting the needs of medical students. He has been handicapped by the availability of suitable paper which has necessitated using one type of paper for the text and another for the illustrations. This has led to the grouping of illustrations separately from the text. The illustrations make full use of the vast amount of clinical material available, but unfortunately in places the reproduction is not clear. The long list of plates at the beginning of the book is rather laborious.

In a book as comprehensive as this it is not surprising that one may disagree with some of the opinions expressed, but there are certain points which call for comment. In the classification of leprosy the distinction between lepromatous, dimorphous and tuberculoid types could be made clearer. When possible, in the prophylaxis of tetanus it would be safer not to use ATS, but to give toxoid covered by a week's course of penicillin which could be given orally. In the management of fluid and electrolyte balance the term 'dextrose/saline' is used a little loosely, and while M/6 lactate is mentioned in the management of acidosis, sodium bicarbonate solution is omitted. Under anaesthesiology, no mention of extradural anaesthesia other than caudal block is made, and there is no mention of the management of diabetes which is so common in South India. External cardiac massage and early intravenous sodium bicarbonate are omitted in the management of cardiac arrest. Compression sclerotherapy for varicose veins is difficult to practise in India, but it should be mentioned under the heading of injection therapy.

An alarming piece of advice is the combination of hyalase with adrenaline for subcutaneous infiltration in thyroidectomy, and no mention is made of the use of propranolol in thyroid crisis. Under hyperparathyroidism it would be correct to say that if hyperplasia is found it involves all the glands. In the management of Stage 1 or 2 carcinoma of the breast no reference is made to simple mastectomy, and under radical mastectomy there is no mention of the Patey type of procedure. The section on hiatus hernia would be more balanced if some space could have been given to surgical procedures. When describing the Ramstedt operation for pyloric stenosis one would not disagree that often in India it is safer to operate under local anaesthesia, but one could well disagree with the statement that 'open ether is safest'. The statement that gastric ulcers are commoner than duodenal ulcer in Africa is not correct. Vagotomy in the management of duodenal ulcer—a big problem in South India—is but briefly presented. Fractional test meals are mentioned, although these have been largely replaced by estimations of maximal acid output when required, but there is no reference to augmented histamine or pentagastrin test meals. Gastroscopy with the rigid instrument is referred to but no mention is made of modern endoscopy.

The description of the management of rectal prolapse is incomplete without reference to the Charles Wells operation or Thiersch's procedure. Excision is advised as the surgical procedure for chronic fissure in ano. One would not agree with the statement that when the serum amylase is raised above 150 Somogyi units acute pancreatitis should be suspected, or with the advocacy of biopsy in chronic pancreatitis. Not all would agree that every case of chronic retention of urine requires slow decompression—it is probably more important that such cases should be adequately hydrated. Such cases could also have a period of preparation by urethral catheter drainage and not all require a two-stage prostatectomy as stated. There is no description of the technique of passing an urethral catheter. Retropubic prostatectomy is not described. Most of us would not excise a congenital hydrocele in small children. Phenoxybenzamine and β-blockers should be given a place in the surgery of phaeochromocytoma.

Despite all these criticisms this book is a monumental achievement, but one wonders whether it would not have been better to have concentrated on the surgical problems which are peculiar to India. Much of the surgery practised in India differs little from that practised in this country. If available locally, it would be hard to improve on some of the well-tried and reasonably priced English textbooks. Such books would provide all the necessary background, and the efforts of experienced Indian surgeons could be directed to producing supplementary textbooks dealing with problems such as abdominal tuberculosis, hydatid disease, splenomegaly, volvulus and leprosy which are commonly found in India.

F. I. TOVEY

Children's Fractures

Mercer Rang, Toronto, and 5 contributors. 278×215 mm. Pp. 238+xiv. Illustrated. 1975. Oxford: Blackwell Scientific Publications. £15·40.

THIS book on children's fractures begins with a parable in the Preface which the reviewer had great difficulty in understanding. In the Acknowledgements the author observed that he had been persuaded that it was a small step to transform material from an instructional course into a book. This must account for the unusual, and often exasperating, use of mixed types of illustrations, of ancient photographs (of Monteggia and Galeazzi) and of cartoons. Indeed the one illustrating Waddell's triad is repeated twice. I do not believe that Andy Capp's form of modern pop art drawings with almost Zip! Zam! Zoom! captions makes a textbook any more interesting or the observations any more definitive, especially at a price of £15·40.

The use of technetium radioactive scanning for diagnosing stress fractures does not appear to be a major breakthrough as suggested in the caption of Fig. 0.1. In growing individuals there are too many uncertainties, and indeed hazards, to balance any refinement in their diagnoses.

This book is certainly not for medical students and residents as it does not contain sufficient detail or statistics to support many of the observations. This is a great pity because it is very obvious that Dr Mercer Rang has had a unique experience over the past 10 years in The Hospital for Sick Children, Toronto. Its immense patient population should provide a challenging opportunity for statistical analysis and follow-up. On reading through the text one had the feeling of stumbling over the chapters on chest, gastro-intestinal and genito-urinary tracts and craniocerebral injuries. The style of writing suddenly changes, becomes quite simple and less than that required for a surgical resident. Even the heading 'Bibliography' becomes 'Recommended reading'.

The bibliography throughout is extensive and modern but even so several authors are mentioned in the text without being given a reference, e.g. Weicz et al. (1973).

The author writes about his relationship with both the injured child and the parents and about his own concern for iatrogenic lesions. Learning of these fundamental reactions best comes during the resident's apprenticeship to his mentor. It is difficult to read and appreciate these very personal reactions without having experienced them or seen how they are handled by the teacher.

This is a very 'personal' book from an obvious expert and surely will have its greatest appeal to those who know Dr Mercer Rang and who have been taught by him.

R. B. DUTHIE

Postgraduate Surgery Lectures 2

Edited John McFarland, Liverpool. 215 × 140 mm. Pp. 122 + ix. Illustrated. 1974. London: The Butterworth Group. £2·65.

This is the second volume in the *Postgraduate Surgery Lectures* series selected from the 1972/73 season at the Liverpool Medical Institution. Eight of the lecturers have presented for publication subjects in which they are expert.

The book opens with a lively chapter on postoperative peritoneal adhesions which represents a useful summary of the subject and practical suggestions. This is followed by the problem of haemophilia in abdominal surgery, the sequelae of head injuries and the problems of testicular tumours. The next chapters deal with obstructive uropathy, cholecystectomy, the controversial subject of the treatment of gastric ulcers and lastly metabolic care in surgery.

This is a readable and enjoyable book, useful for FRCS candidates and all who are interested in general surgery.

IAN MCCOLL

A Guide to Disaster Management based on Proceedings of an Inter-service Conference held in the Walton Conference Centre, The Southern General Hospital, Glasgow, in September 1973, and a Report on Disaster Response in America and Canada following the Tornadoes of April 1974.

Edited W. Sillar, Glasgow. 298 × 210 mm. Pp. 115. 1974. Glasgow: Action for Disaster. £2.

With the publication of this book, another valuable contribution has been made to disaster technology. In 1973 Action for Disaster, a Scottish voluntary organization concerned with the saving of human life, arranged a meeting in Glasgow of representatives of all emergency services to discuss disaster management. Both the police and fire service spokesmen emphasized the importance of defining roles and areas of responsibility and the need for liaison, communication and agreement over command in disaster management, but the representative of the ambulance service drew attention to the fact that the role of his service in casualty care, as well as transportation, was often not fully appreciated by the other emergency services.

Two papers of particular interest to clinicians will be those from Swedish contributors: 'The Role of the Medical Services' and 'The Doctor at the Disaster Site'. The book also includes a report on a visit made by the Editor and a colleague to North America to study the disaster response following a number of tornadoes. Many of the lessons learned the hard way by others have yet to be applied to disaster planning in the United Kingdom.

P. E. A. SAVAGE

Tumors of the Major Salivary Glands (Atlas of Tumor Pathology, Second Series)

A. C. Thackray and R. B. Lucas, London. 260 × 200 mm. Pp. 144 + xii, with 163 illustrations. 1974. Washington, DC: Armed Forces Institute of Pathology. $8.85.

The publication of this book has been an important event in surgical pathology. One fascicle of the second series of the *Atlas of Tumor Pathology* that is being published by the United States Armed Forces Institute of Pathology under the general editorship of Dr H. I. Firminger, it describes the various lesions that may present as a lump in a salivary gland in terms of the World Health Organization scheme for the 'Histological Typing of Salivary Gland Tumours'. Professor Thackray was, of course, one of the authors of that scheme, and the publication of this book so soon after the scheme itself should do much to consolidate the position of this classification as the premier choice of pathologists all over the world.

After an introduction concerned with embryology, anatomy and physiology, the various tumours are described under the general headings of definition, clinical features, histogenesis, gross and microscopic appearances, treatment and prognosis and differential diagnosis. The illustrations are marvellously clear, whether one looks at the 155 black and white figures or the 8 illustrations in colour.

The whole book is imbued with the personality of the authors, who describe pathology not as an end in itself but as a way to a better understanding of how a patient should be treated. There are wise remarks on the pitfalls of trying to make a histological diagnosis from small fragments of a tumour (such as may be produced by drill biopsy), on the dangers of attempting to cure a pleomorphic adenoma by enucleation and on the value of radiotherapy as an adjunct to excision in the more malignant lesions.

All in all, no one who is particularly interested in the management of patients with salivary gland tumours can afford to do without this book; it is cheap at the price.

MICHAEL HOBSLEY

Sémiologie Chirurgicale

Lucien Léger, Paris. 270 × 215 mm. Pp. 480 + xiii, with 989 illustrations. 1974. Paris: Masson et Cie. 100F.

This is an interesting book and primer to surgical studies, relating the presentation of the patient and the clinical signs, all illustrated with appropriate line drawings and radiographs of good quality interspersed with apposite statements tinged with Gallic wit.

It covers the whole field of surgery including gynaecology but excluding ophthalmology and otorhinolaryngology. It can be strongly recommended to preclinical students as, by means of short sentences with descriptive drawings, it teaches basic orthodox surgery and pathology.

Unfortunately, it would probably not bear translation because of the excellence of similar books in the English language, but it satisfies a very real need in France and French-speaking countries. The preface is notable for the comment on continuing changes in the syllabus and lack of facilities for students to see clinical material—a comment apposite for this country as well.

JEAN CLAUDE GAZET

Trauma Management

Edwin F. Cave, John F. Burke and Robert J. Boyd, Massachusetts. 253 × 180 mm. Pp. 1237 + xviii. Illustrated. 1975. London: Lloyd-Luke. £42·75.

I do not know what to say about this book. Partly this is because its original inspiration and continued bias are orthopaedic and I am not skilled in that field; partly because I recoil from the expensive production on hyperglossy paper; partly because I find it difficult to conceive of who would buy a book in a changing subject which costs what this one does; partly because in spite of the monumental price my review copy was delivered with a number of flawed pages. Never was so little offered in so much bulk at such a price.

These things said and spleen vented, what has this book to offer? There are reasonably up-to-date, well-written accounts of the metabolic response to injury, largely the responsibility of Dr Burke; exhaustive treatment of fracture problems, with, as might be expected in a centre like the Massachusetts General, a considerable emphasis on the patient who has gone wrong elsewhere. The approach to areas where I have greater familiarity seems less complete, which makes one doubt the overall authority of the work. Seat belt visceral injuries and chance vertebral fractures I could not find. Selective approach to civilian penetrating abdominal injury is dismissed. Stress ulceration merits only a paragraph and treatment is not considered. Acute acalculus cholecystitis is not mentioned in spite of the Vietnam experience. All in all the vaulting ambition of this book has o'er leaped itself.

Even if we do not insist on the comprehensive text—to which we might feel entitled in view of the weight and price—it is possible to cavil at the failure to give definite advice on what to do or how to reach a decision. All too often every possibility is listed without a firm recommendation being made, as if the writer was anxious to display erudition without exercising responsibility.

The volume may go down in history as a monument to the industry of its contributors but it will little advance the scholarship of surgery.

H. A. F. DUDLEY

Soviet Research in Pharmacology and Toxicology
William H. Fitzpatrick. 230 × 150 mm. Pp. 322+xii. 1974. Maryland: US Department of Health, Education and Welfare. $3.05.

THIS book is a publication of the John E. Fogarty International Center for Advanced Study in the Health Sciences. It was published in 1974 and is supported by the US Department of Health, Education and Welfare, Public Health Service, National Institutes of Health. Its aim is to examine the subject so that others may have a better perspective of work in the field in the USSR. A secondary objective is to encourage co-operation between health scientists and administrators of various countries.

The book covers a wide range of subjects in pharmacology and toxicology. Those involved in research will be well aware of much of the Soviet work because these articles are cited in many abstracting journals, often with a brief English summary. It seems unlikely that the contents will be of particular interest to surgeons, as might be expected from the title. Its main use would be to give a broad view of the kind of work going on rather than to give information in depth on any particular line of research.

J. G. MURRAY

Alexis Carrel. Visionary Surgeon
W. Sterling Edwards and Peter D. Edwards, Albuquerque, New Mexico. 230 × 150 mm. Pp. 143+x, with 15 illustrations: 1974. Springfield, Ill.: Charles C. Thomas. $5.

THE life of Alexis Carrel was full of interest, for he was not only a great scientist and practical surgeon but also a mystic. Carrel has been called the father of vascular surgery because of his techniques of arterial suture and blood vessel grafts.

There are still many surgeons who remember Carrel's irrigation apparatus, which was extensively used in the First World War in the treatment of septic wounds and gas gangrene.

Charles Lindleigh, who was a co-worker of Carrel in many of his investigations, writes a laudatory foreword to this biography.

Professor Sterling Edwards and his son Peter have put the medical profession in their debt by writing this excellent biography. It must not be forgotten that Carrel's Nobel Prize in Surgery was a token of his international regard, for he had a most original and stimulating mind. Although he was the first to produce an artificial heart, he was also responsible for techniques of tissue culture. A very versatile and exceptional surgeon.

CECIL WAKELEY

Book notices

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and those having the greatest interest to our readers.]

Regulation of Gene Expression in Eukaryotic Cells
Edited Maureen Harris and Brad Thompson. 230 × 150 mm. Pp. 127+vi. Illustrated. 1974. Maryland: US Department of Health, Education and Welfare. $4.15.

National and Regional Health Planning in Sweden
Vicente Navarro, Baltimore. 230 × 145 mm. Pp. 244+xvii, with 35 illustrations. 1974. Maryland: US Department of Health, Education and Welfare. $2.55, paper covers.

Fonctions et Bilans Articulaires
Ch. Rocher and A. Rigaud, Bordeaux. Third edition. 160 × 240 mm. Pp. 320, with 215 illustrations. 1974. Paris: Masson et Cie. 76F.

Soviet Biomedical Institution: A Directory
A publication of the Geographic Health Studies Program of the John E. Fogarty International Center for Advanced Study in the Health Sciences prepared under an Interagency agreement with the Library of Congress. 268 × 105 mm. Pp. 553+xviii. 1974. Maryland: US Department of Health, Education and Welfare. $5.95.

Diseases of the Esophagus. Volume 3
G. Vantrappen, J. Hellemans and contributors. 248 × 168 mm. Pp. 877, with 358 partly coloured illustrations. 1974. Berlin: Springer-Verlag. DM.390.

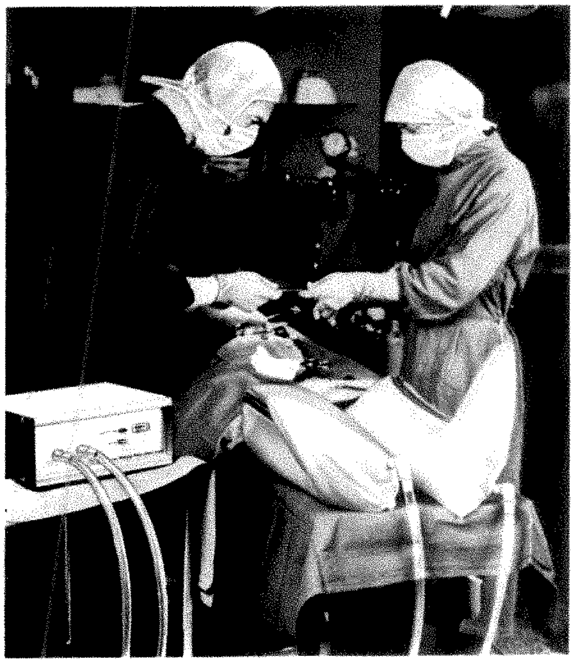
New Parts for Old, the Age of Organ Transplants
John G. Deaton, Austin, Texas. Pp. 160. Illustrated. 1974. Palisade, New Jersey: Franklin Publishing Co. Inc. $7.40.

Metabolic Disorders of Bone
C. R. Paterson, Dundee. 232 × 155 mm. Pp. 373+x. Illustrated. 1975. Oxford: Blackwell Scientific Publications. £8·25.

The ABC of Acid–Base Chemistry
Horace W. Davenport, Chicago. Sixth edition. 150 × 225 mm. Pp. 124+vii. Illustrated. 1974. London: University of Chicago Press. Cloth £4·25; Paper £1·75.

Smooth Muscle Regeneration. (Monographs in Development Biology)
John K. McGeachie, Nedlands, Western Australia. (Series editor A. Wolsky.) 225 × 155 mm. Pp. 90+vii, with 39 illustrations. 1974. Basel: Karger. No price given.

BOC Roberts Venous Flow Stimulator tackles the problem of d.v.t. where it starts



Every patient undergoing surgery is at risk from deep vein thrombosis. According to the Registrar General's reports, the incidence of death from d.v.t. - induced post-operative pulmonary embolism, is steeply rising.

It has been demonstrated* that the occurrence of deep vein thrombosis can be dramatically reduced by the application of intermittent calf compression per-operatively to prevent venous stasis. This procedure is, however, successful only when the pressure cycle conforms to blood flow dynamics. Critical considerations are:

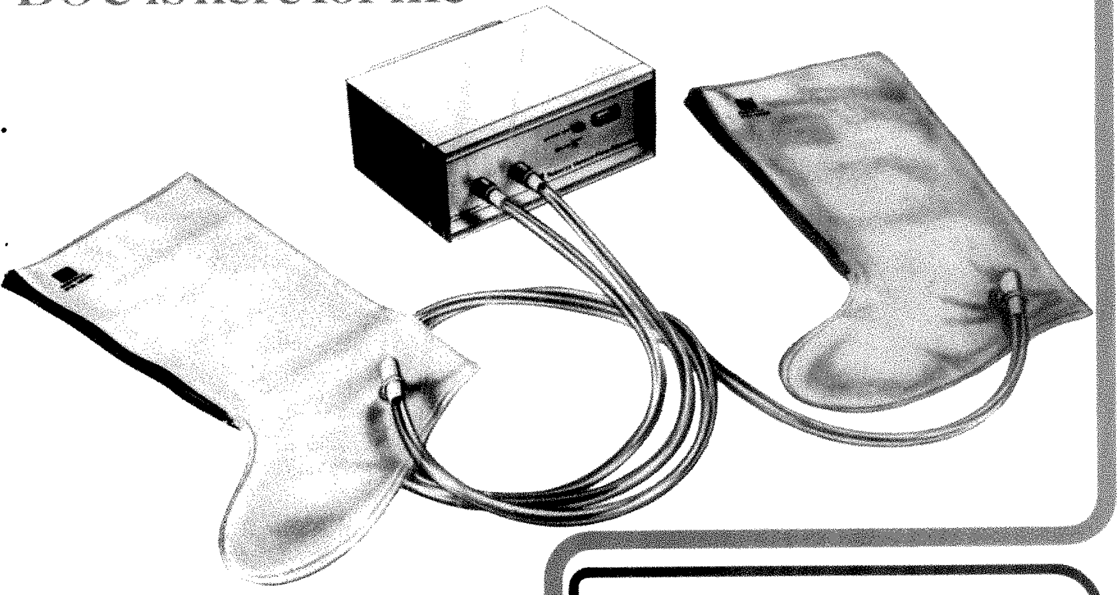
- ● The duration and magnitude of the applied pressure.
- ● The timing of the pressure cycle to give vessels the optimum time to refill between compression phases.

Only the BOC Roberts Venous Flow Stimulator meets these criteria precisely and automatically. Clinical trials indicate that the apparatus can eliminate over 75% of cases of post-operative d.v.t. without the need for chemical intervention.

If you would like to know more about this equipment, please write or telephone us at the address below.

*Roberts, V.C. and Cotton, L.T. (1974a) British Medical Journal 1 358

BOC is here for life



BOC Medishield
Elizabeth Way Harlow
Essex CM19 5AB England
Telephone Harlow (0279) 29692
Cables Britoxygen Harlow
Telex 81479

☐ Please send me details of the BOC Roberts Venous Flow Stimulator.

Name ....

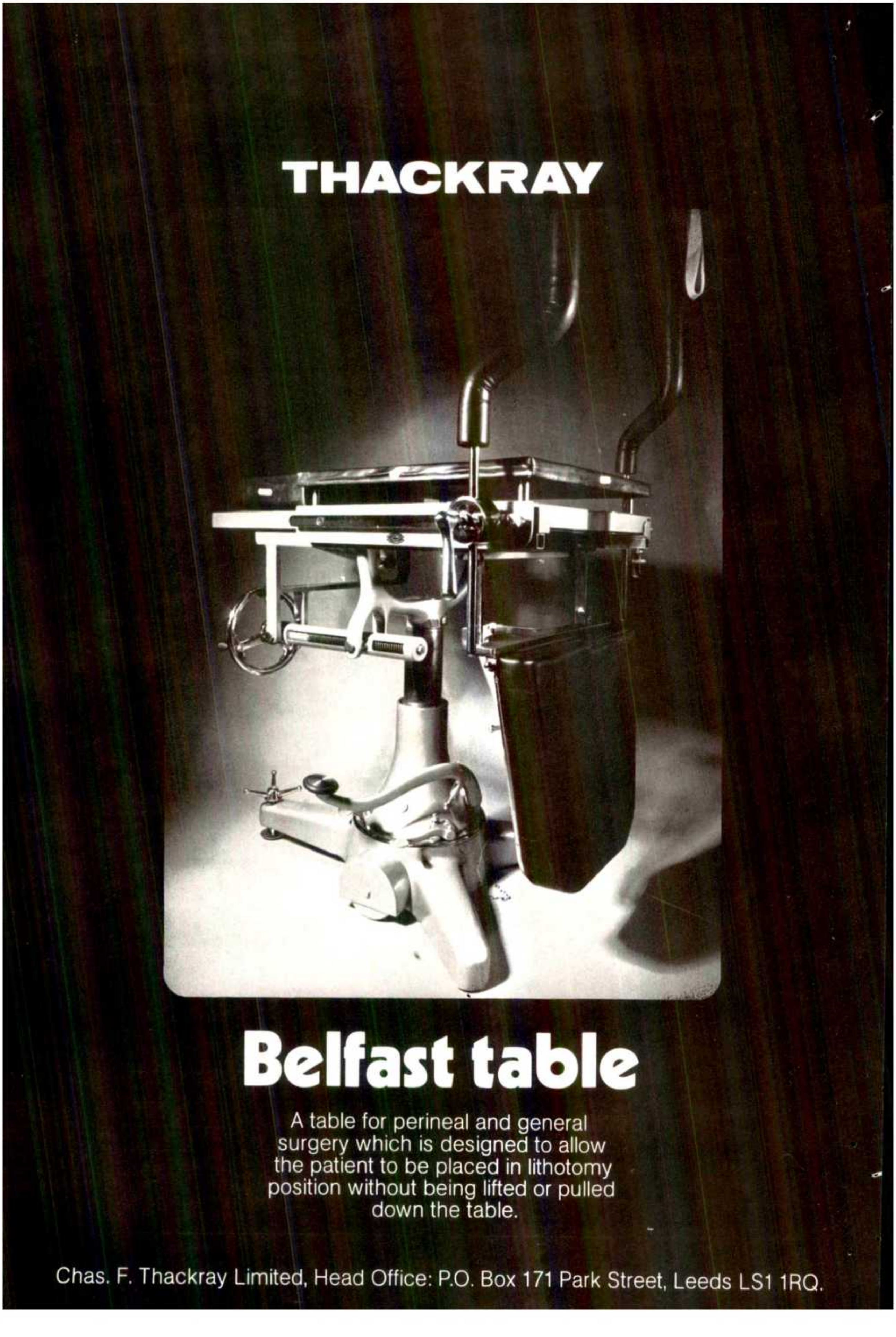
Position ....

Hospital ....

Address ....

....

BJS



Belfast table

A table for perineal and general surgery which is designed to allow the patient to be placed in lithotomy position without being lifted or pulled down the table.

Chas. F. Thackray Limited, Head Office: P.O. Box 171 Park Street, Leeds LS1 1RQ.

What's so different about a routine foley catheter?

At a glance the new Simplastic foley catheter is different – it's the clear PVC one. For your patients the difference is simply that they're more comfortable.

- The extra-large lumen size of SIMPLASTIC foley catheters allows smaller gauges to be selected, thereby reducing urethral trauma and the risk of infection. Just compare a 22Ch latex catheter with a 16Ch Simplastic foley catheter – the internal lumen sizes are almost identical.

- Easy to insert, SIMPLASTIC foley catheters are soft and supple at body temperature providing maximum patient comfort.
- Made from implant tested PVC, SIMPLASTIC foley catheters are less likely to cause urethral irritation.

The new
SIMPLASTIC
routine-use foley catheters
Simply better for your patient

J. G. Franklin & Sons,
P.O. Box 11, High Wycombe, Bucks.,
HP12 3TD, England.
A division of G. D. Searle & Co Ltd.

Further information will be supplied promptly upon request

Simplastic is a registered trade mark

INJURY

The British Journal of Accident Surgery

Editor, R. L. BATTEN, FRCS(Eng)

Injury provides a focal point of information for those engaged in the many fields of medicine which accident surgery involves. Contributions from all over the world provide well-organized and comprehensive coverage of every aspect of care of the injured. Original articles take up a large section of INJURY and, as accident surgery is so often concerned with the individual patient, reports of interesting and complex cases are included. To keep the reader informed of the latest progress, INJURY contains details of current research and of new drugs and medical instruments. Reviews of new books appear regularly and, of particular value in a field of medicine which often has a debt to other specializations, INJURY devotes some of its space to abstracts from a wide range of publications on related subjects.

Published Quarterly

Annual Subscription: £10·00 (post free)

Single Numbers: £3·00 (post free)

BURNS including Thermal Injury

The Journal of the International Society for Burn Injuries

Editor, J. E. LAING, FRCS

To counter the high mortality and morbidity caused by burn injuries needs the teamwork of a wide range of specialists: treatment of the patient can involve plastic, paediatric and orthopaedic surgeons, biologists, immunologists and bacteriologists, while the rehabilitation of the patient can need the efforts of occupational therapists, physiotherapists, psychiatrists and social workers. This new journal is published to foster the exchange of information amongst all those engaged in preventing and minimizing the effects of burn injuries. BURNS is sponsored by the International Society for Burn Injuries, whose aims are to transcend national boundaries in improving the prevention and care of burns by education, research, practical advice and assistance, and the encouragement of cooperation between all countries and all specialists.

Published Quarterly

Annual Subscription: £10·00 (post free)

Single Numbers: £3·00 (post free)

JOHN WRIGHT

42–44 Triangle West, Bristol BS8 1EX

ARMOUR TEMPORARY BIOLOGICAL DRESSING CAN SOLVE THE IMMEDIATE PROBLEM OF TISSUE LOSS COVERAGE AND REPAIR

effective in the treatment of

- partial thickness burns
- debrided full thickness burns
- traumatic skin loss injuries
- soft tissue defects
- decubitus and vascular ulcers

The many advantages of using a biological dressing are

- dramatic reduction of pain
- reduction of fluid and protein loss
- reduction of heat and energy loss
- reduction of infection
- increase in mobility
- protection of exposed tendons, vessels and nerves
- promotion of healing
- psychological improvement of the patient
- improvement of scarring
- In full thickness burns, used as a "test material" to predict the readiness of the granulating bed to accept autograft. This results in a more economical use of autograft material.

Armour porcine skin dressings are presented in sterile lyophilised form, can be conveniently stored without refrigeration and may be reconstituted prior to use in sterile water or balanced electrolyte solution.

Package and size availability is as follows:
Boxes of 5 x 1 sq. ft. roll 3″x 48″
Boxes of 5 x ¼ sq. ft. roll 3″x 12″
Boxes of 10 Patches 2½″x 4″
Boxes of 5 x Wide Strip 8″x 18″
Boxes of 5 x Wide Half Strip 8″x 10″

Full product information on request from
Armour Pharmaceutical Company Limited
Eastbourne Sussex England BN22 9AG

JA6/ABD/5

PRE-WAR TOY TRAINS

Wanted for local museum Bing, Hornby and Bassett-Lowke tinplate trains—clockwork, electric or steam, including any accessories however small. Condition is not important as often one piece can be used to restore another. We are aiming to set up as complete a collection of pre-war models as possible, and welcome any relevant items. Reasonable prices paid.

P. B. WHITEHOUSE J.P., Birmingham Railway Museum, 5 Birch Hollow, Edgbaston, Birmingham B15 2QE. *Tel.:* 021 454 7395.

BRITISH JOURNAL OF SURGERY

Binding Cases

Binding cases for Volume 61 may be obtained from the Publishers at £2·00 post free. They are supplied in dark blue cloth with imitation gold lettering on the spine.

If desired, the publishers will undertake the binding at an inclusive charge of £7·50, post free.

JOHN WRIGHT

42–44 TRIANGLE WEST, BRISTOL BS8 1EX

New and Revised 11th Edition

AUGUST

Synopsis of Surgical Anatomy

Edited by D. J. du PLESSIS
CHM (Rand), FRCS (Eng)

Head of the Department of Surgery, University of Witwatersrand, Johannesburg; Chief Surgeon, Johannesburg General Hospital

A general revision has been undertaken to bring the whole book up to date and also to eliminate those sections which were not absolutely essential because it is important to prevent a book of this type from becoming too large. This new completely revised edition, with many excellent illustrations, is in two parts: Anatomy of the Normal and Anatomy of the Abnormal.

898 pages 779 illustrations £7·00 net

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

Our experience is something you can rely on

Remploy's contribution to Orthotics goes far beyond providing a comprehensive range of orthopaedic equipment.

Remploy are able to offer a unique measuring and fitting service for all their appliances and footwear, and have produced two orthopaedic brochures which are an invaluable aid to work in this field. Rely on this experience and send for literature, now.

Remploy

An exceptional name in Orthotics

A.H. Knight Remploy Limited (Orthopaedic Division),
Remploy House, 415 Edgware Road, Cricklewood,
London NW2 6LR. Telephone: 01-452 8020.

Physical Examination of the Surgical Patient:

An Introduction to Clinical Surgery 4/e

By J. Engelbert Dunphy, M.D., Professor of Surgery, University of California School of Medicine, San Francisco, California, and Thomas W. Botsford, M.D., Associate Professor of Surgery, Harvard Medical School.

This fourth edition of **Physical Examination of the Surgical Patient** has undergone extensive revision, and introduces such new emphases as the problem orientated record and pathophysiologic mechanisms of surgical disease. Major changes to this edition appear in the elective examination of the breast, heart, abdomen, and the cancer patient; the emergency examination of the chest, abdomen, and the thermally injured patient. A more clear and concise listing of supplementary readings replaces the old bibliography, and many of the older figures have been replaced with new ones. A second colour plate of epidermal lesions has also been added.

430pp 215 illustrations (2 pages in colour) Cloth binding Price £8.85
Published March 1975

Surgery in the Aged

A title in the series Major Problems in Clinical Surgery

By Lazar J. Greenfield, M.D., Professor of Surgery, The University of Oklahoma Health Sciences Centre College of Medicine, Oklahoma City, Oklahoma.

Approx 250pp Illustrated Cloth binding Approx price £6.65
Publication date September 1975

Atlas of Vaginal Surgery

By Frederick J. Hofmeister, M.D., Associate Clinical Professor, Department of Gynaecology and Obstetrics, Medical College of Winsconsin.

225pp Illustrated Cloth binding Price £8.30 Published January 1975

Surgery of the Trachea

By Hermes C. Grillo, M.D., Massachusetts General Hospital, Boston Massachusetts.

200pp Illustrated Cloth binding Price £7.75 Published January 1974

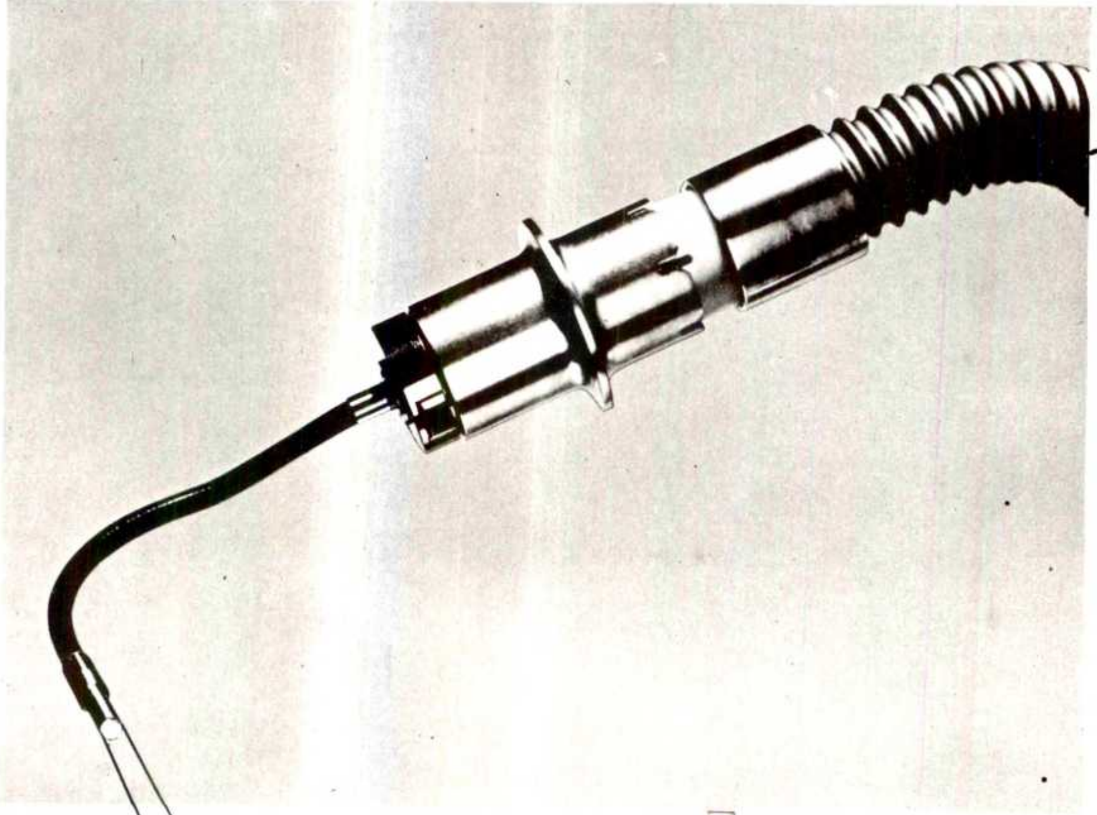
To obtain your inspection copy, write now to Colin Dann–Publicity Manager, 120 Golden Lane London EC1Y 0TU–Please quote reference WBS 9 with your reply.

W. B. Saunders Company Ltd
12 Dyott Street London WC1A 1DB

new

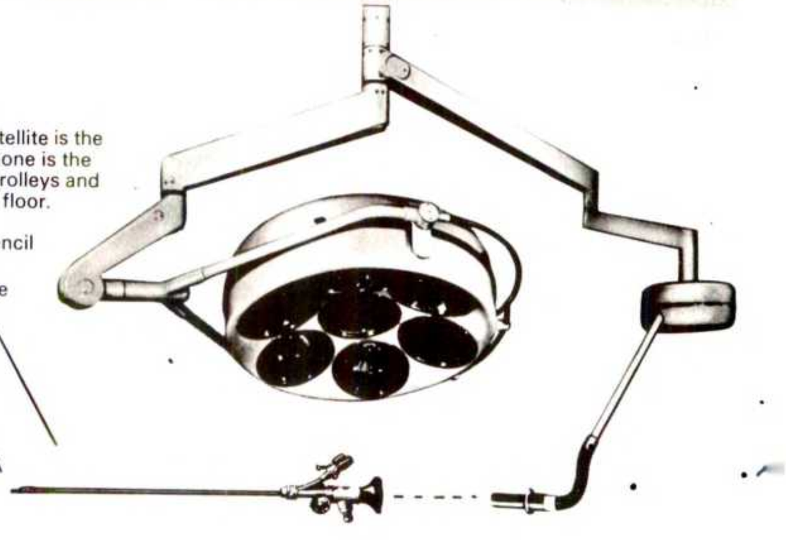
SIEREX

FLEXIBLE PENCIL LIGHT



The Boston lamp with its GFO Satellite is the ideal endoscopic light source. Gone is the need for a separate source, for trolleys and mains cables trailing across the floor.

Illustrated above is a flexible pencil light, ideal for Neuro and ENT surgery, shown connected to the GFO Satellite.



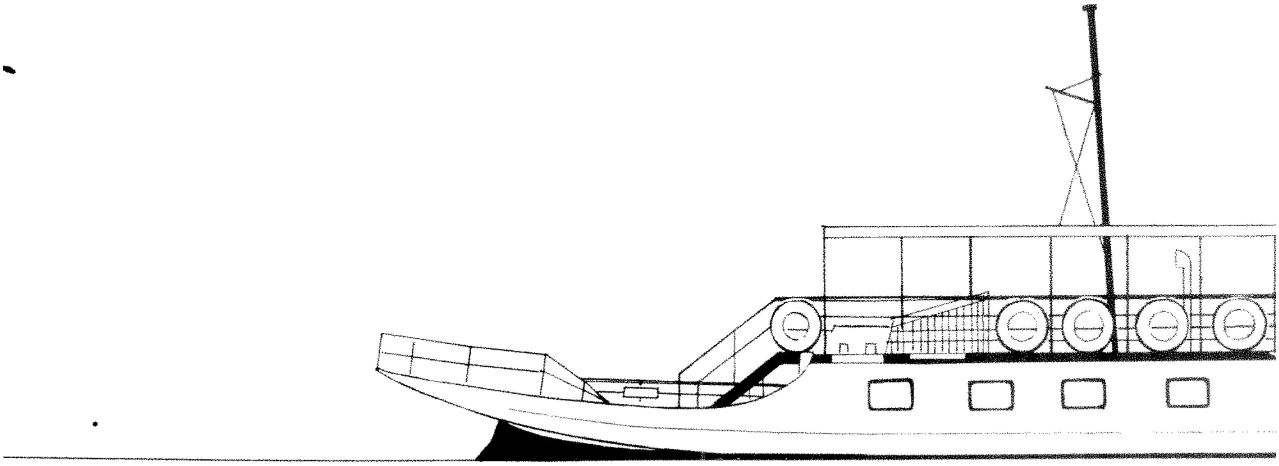
Most glass-fibre endoscopic instruments can be connected in this way.

Sierex

Sierex Limited

15/18 Clipstone Street, London, W1P 8AE, 01-580 2464
Branches in *Aberdeen, Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester and Reading.*
Agents in *Belfast, Newcastle and Newport.*

Missed it?

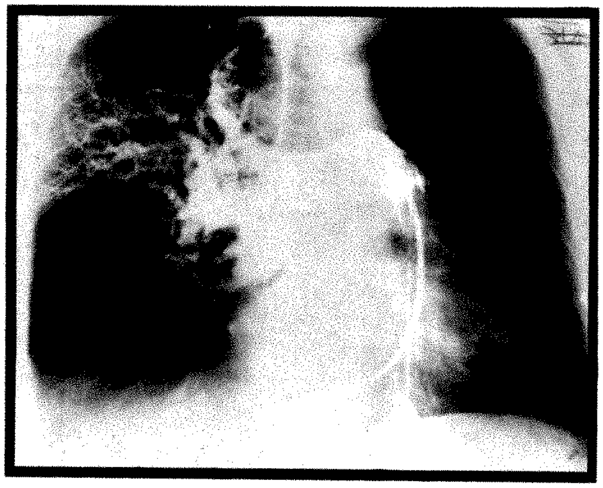


Aminoplex 5
Aminoplex 14
Aminutrin
Calonutrin
Nefranutrin

Geistlich Nutrition

Geistlich Sons Limited Chester

RED ALERT!



When acute massive pulmonary embolism occurs put them on Kabikinase to dissolve the embolus and the still threatening deep vein thrombus and restore the flow. (Lysis achieved, anticoagulate with heparin to prevent rethrombosis.)

"We believe that the current treatment of choice for most cases of acute life-threatening pulmonary embolism is streptokinase." 1

1 Comparison by Controlled Clinical Trial of Streptokinase and Heparin in Treatment of Life-threatening Pulmonary Embolism. Brit. med. J. **1.** 343 (1974).

KABIKINASE

(pure streptokinase)

Full information, brochure and wall card on request.

Kabikinase is manufactured by AB Kabi, Stockholm, Sweden, and is available only from:

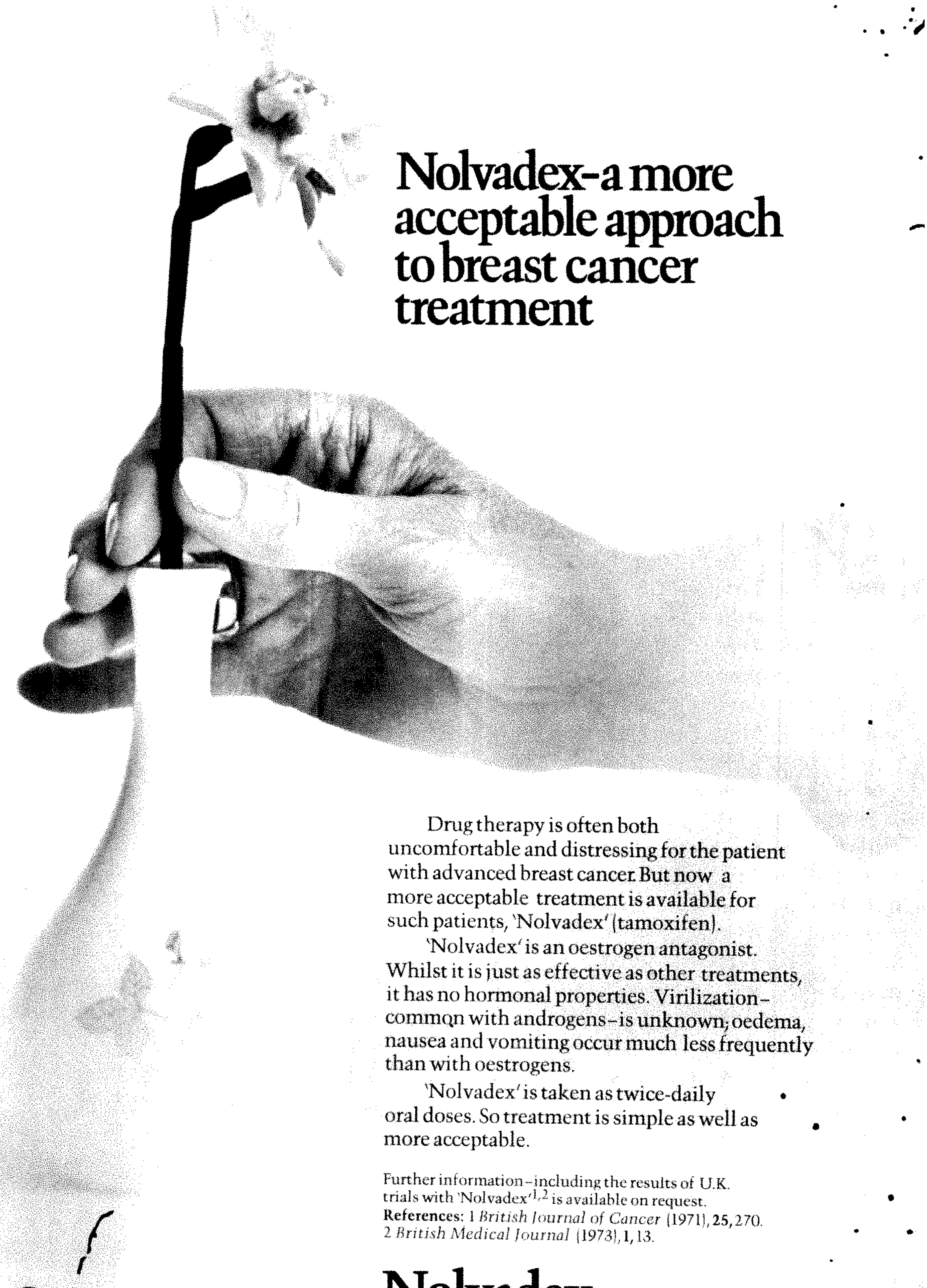
KabiVitrum

KabiVitrum Limited,
Bilton House,
Uxbridge Road,
London W5 2TH
Telephone: 01-567 4717 01-579 1871

P.L. No. 0022/5006
Kabikinase is a registered trade mark.

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU

Nolvadex–a more acceptable approach to breast cancer treatment



Drug therapy is often both uncomfortable and distressing for the patient with advanced breast cancer. But now a more acceptable treatment is available for such patients, 'Nolvadex' (tamoxifen).

'Nolvadex' is an oestrogen antagonist. Whilst it is just as effective as other treatments, it has no hormonal properties. Virilization–common with androgens–is unknown; oedema, nausea and vomiting occur much less frequently than with oestrogens.

'Nolvadex' is taken as twice-daily oral doses. So treatment is simple as well as more acceptable.

Further information–including the results of U.K. trials with 'Nolvadex'[1,2] is available on request.
References: 1 *British Journal of Cancer* (1971), 25, 270.
2 *British Medical Journal* (1973), 1, 13.

Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

Nolvadex

Easier to give, easier to take

'Nolvadex' is a trade mark

Vol. 62 : No. 9 : September 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
I. D. A. JOHNSTON Newcastle
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN McADAM Kampala : Uganda
A. C. McEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX
Subscription £15 per annum, post free. Single copies £1·50, post free

---

THE WILLIAMS & WILKINS CO., BALTIMORE
Subscription $36·00 per annum. Single copies $3·00
Second Class Postage paid at Baltimore, and at additional mailing offices.

NOW
MORPHINE
MINUS
VOMITING

CYCLIMORPH

TRADE MARK

CYCLIMORPH Injection has all the benefits of morphine plus an effective anti-emetic, cyclizine – in a single injection.

Cyclizine significantly reduces the incidence of nausea and vomiting,[1] whether associated with the condition or morphine-induced.

CYCLIMORPH is indicated in all conditions where morphine is needed.

[1] *Br. J. clin. Pharmac*, (1975). 2, 81.

Full prescribing information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd.
Berkhamsted, Herts

The British Journal of Surgery

Vol. 62: No. 9: September 1975

Original papers

		Page
Whither thyrotoxicosis?	W. Michie	673
Surgical treatment of thyrotoxicosis: results of 272 operations with special reference to preoperative treatment with anti-thyroid drugs and L-thyroxine	Peter Heimann and Jan Martinson	683
Carcinoma arising in thyroglossal duct remnant: case reports and review of the literature	Prakash C. Saharia	689
Secondary carcinoma of the thyroid gland	John A. Thomson, J. S. Kennedy, M. K. Browne and J. Hutchison	692
The significance of occult skeletal metastases, detected by skeletal scintigraphy, in patients with otherwise apparently 'early' mammary carcinoma	C. S. B. Galasko	694
Acute cholecystitis	P. A. M. Raine and A. A. Gunn	697
Prognosis after portocaval anastomosis: a 15-year follow-up	R. Windle and J. H. Peacock	701
The effect of acute ethanol administration on the exocrine pancreatic secretion of the pig	I. C. Wheatley, G. O. Barbezat, Rosemary Hickman and J. Terblanche	707
The effect of heparin and of acid-citrate-dextrose solution on screen filtration pressure of blood in experimental hypotension	B. J. Pardy and H. A. F. Dudley	713
Acute segmental ischaemic enteritis in Thailand	Theodore P. Welch and Somsak Sumitswan	716
Cause and management of high volume output salt-depleting ileostomy	G. L. Hill, W. S. J. Mair and J. C. Goligher	720
Factors influencing local recurrence after abdominoperineal resection for cancer of the rectum and rectosigmoid	A. R. Moossa, P. C. Ree, J. E. Marks, B. Levin, C. E. Platz and D. B. Skinner	727
The transdiaphragmatic approach to the heart	E. W. J. Cameron	731
False abdominal aortic and iliac aneurysms	Demetrios Chavatzas and Crawford Jamieson	734
Gastric acid secretion following renal transplantation	J. S. F. Canavan, J. D. Briggs and P. R. F. Bell	737
Collagen biosynthesis in normal and hypertrophic scars and keloid as a function of the duration of the scar	R. D. Peter Craig, J. David Schofield and David S. Jackson	741
A technique for re-exploration of the saphenofemoral junction for recurrent varicose veins	Arthur K. C. Li	745
Parathyroid indentification by methylene blue infusion	Donald L. Gordon, Mohan C. Airan, William Thomas and Leon H. Seidman	747
Selective surgery for abdominal stab wounds	A. Thavendran, A. Vijayaragavan and Rudra Rasaretnam	750
Reviews and notices of books		753

© John Wright & Sons Ltd and the respective contributors named above, 1975.

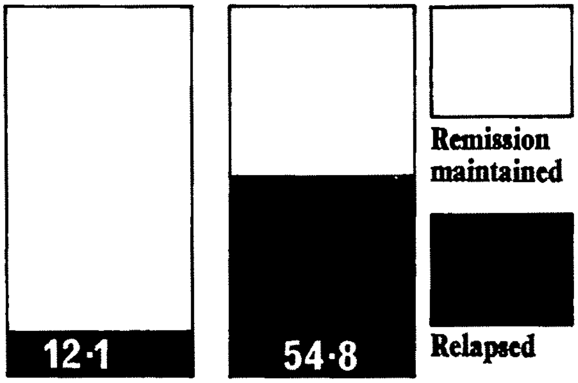
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any other form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.

"It is concluded that maintenance treatment of ulcerative colitis with sulphasalazine (salazopyrin) should be continued indefinitely unless contraindicated by side effects".[1]

The results of the above controlled trial carried out at the Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, are all the more welcome as earlier trials of cortisone[2] and prednisone[3] at standard dosages have shown them to be totally ineffective in reducing the number of recurrences of ulcerative colitis.

"Fortunately, Sulphasalazine tablets, 0.5 grams, 4 times a day will prevent relapses in the majority of patients with colitis, and only a few patients cannot tolerate this relatively small dose, which can be continued indefinitely, since we do not know when, if ever, it can be safely stopped".[4]

"A striking difference in the relapse rate".



"The patients who received dummy tablets had more than four times the relapse rate of those receiving sulphasalazine".[1] (Salazopyrin).

Salazopyrin (sulphasalazine) is available as the plain 0.5 g. tablet, 0.5 g. EN-tab and as an 0.5 g. suppository. Literature and detailed information on Salazopyrin are available on request.

References
1. Gut (1973) 14 923–926
2. Brit. med. J. (1959) 1 387–394
3. Lancet (1965) i 188–189
4. General Practitioner (1972) April 7 p11.

Salazopyrin — to be continued indefinitely

Further information available from:—

Salazopyrin is a registered trade mark.

Pharmacia (Great Britain) Ltd.,
Paramount House,
75 Uxbridge Road,
London W5 5SS.
Telephone: 01-579 0102/7

Pharmacia

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original *illustrations* are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 61. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISEMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended. Leaflets giving further instructions are available on request.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

PRESENTATION OF STATISTICS

Authors are reminded that with the frequent use of statistical analysis in biological writing of all kinds it is desirable that:

a. The methods section of a paper should contain a mention of any statistical technique used. If the method is new or unfamiliar either a reference should be given or a description included as a brief appendix.

b. If alternative techniques could have been applied to the data, a short justification of the method is often appropriate.

c. In clinical trials the confidence or tolerance limits of the results should be quoted, particularly when formal statistical significance at the 5 per cent level is only just reached.

d. Abbreviations for statistical terms should follow those used in *Documenta Geigy Scientific Tables*, 7th edition, 1970.

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are more than two authors these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated.

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature (Lond.)* **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea **4**, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th 3d. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology.* London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BLAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

Congress Proceedings

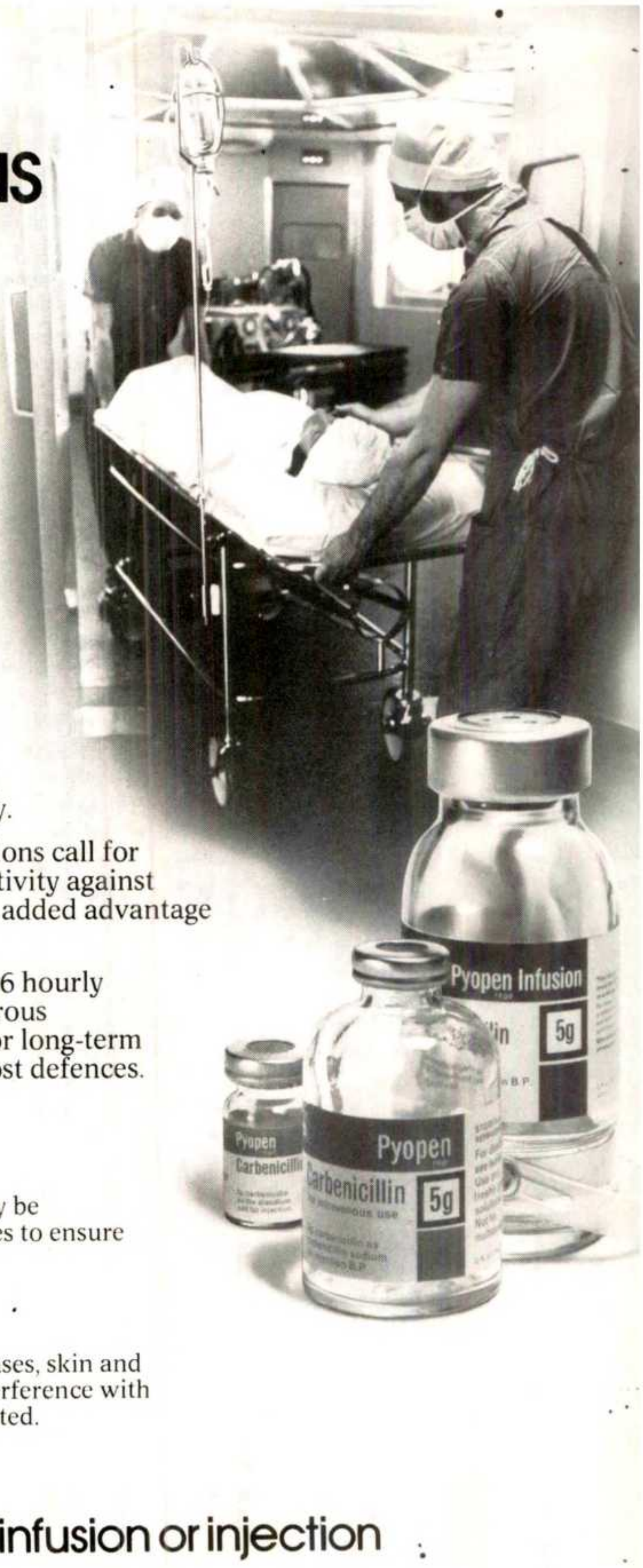
CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding, or that following.

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)

When pseudomonas threatens...



Pyopen

The skill of the surgical team,
hours in the theatre, the most advanced
techniques in the world . . . and infection
can still throw the outcome into jeopardy.

Systemic pseudomonas or proteus infections call for Pyopen. Only Pyopen offers you good activity against these Gram-negative organisms with the added advantage of penicillin safety.

Intravenous Pyopen, at a dosage of 5g 4–6 hourly will rapidly control many of these dangerous infections. And Pyopen is also suitable for long-term therapy and for patients with lowered host defences.

Adult Dosage
5g I.V. 4–6 hourly.
In patients with renal impairment dosage may be reduced; monitoring is advisable in these cases to ensure adequate serum antibiotic levels.
Contra-indication
Penicillin hypersensitivity.
Side-effects
As with other injectable penicillins. In rare cases, skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Pyopen–by infusion or injection

Further information is available on request.
Pyopen* (carbenicillin sodium B.P.) is a British product originated by
Beecham Research Laboratories, Brentford, England. *regd.

SIEMENS

DIATHERMY EQUIPMENT
for modern
ELECTRO-SURGICAL
TECHNIQUES

Available in various designs such as

TROLLEY MOUNTED,
CEILING SUSPENSION
or installation in the
OPERATING THEATRE WALL

Full details available on request

Sierex

SIEREX LIMITED Electro-Medical Department,
Heron House, 109 Wembley Hill Road,
Wembley HA9 8BZ Telephone 01 903 0418

Branches in Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester, Newcastle and Reading. Agents in Belfast.

CHARLES C THOMAS • PUBLISHER

PATHOLOGY AND SURGERY OF THE SALIVARY GLANDS *by* **Jose Yoel**, *Rawson Hospital, Municipal Post Graduate School of Medicine, Buenos Aires, Argentina. Forewords by* **Pierre Cernea**, **John Conley**, **Hector Marino** *and* **S. L. Perzik.** The clarity of the text matter in this book reveals a deep knowledge of the topic under consideration, based on a long and eclectic experience. Anatomy, physiology, pathology and semiology, instrumental and radiological exploration, and medical and surgical treatment of salivary gland diseases have been assigned ample chapters in which every detail has been clearly covered. Clear anatomophysiologic sketches and magnificent illustrations of the operative stages clearly depict what the surgeon actually sees in the operative field. The author's punctilious attention to the surgery of tumoral processes does not lose sight of the possible morphological and functional repair of its consequences. Part I deals with fundamental concepts on embryology, histology, physiology and endocrinology and reviews the general pathology of the salivary glands and their diagnostic methods. Part II details the special pathology of the parotid gland and its excretory duct, the inflammatory condition, different salivary syndromes, lithiasis, primary and metastatic blastomas, as well as blastomas and pseudoblastomas of the parotid area. Parts III, IV and V are concerned with the special pathology of the submaxillary gland and its excretory duct, the special pathology of the sublingual gland, and the special pathology of the minor or accessory salivary glands. Each part contains a chapter on the surgical complications and sequelae. Operative techniques are shown in atlas form on the basis of photographs and notes taken by the artist present at the operation. Numerous photographs of patients as well as x-ray prints, including the reproduction of sialograms, contribute toward illustrating the subject matter. This treatise on the pathology and surgery of the salivary glands will find a wide acceptance since patients with salivary conditions are seen daily by clinicians and dentists, otolaryngologists, stomatologists, maxillofacial surgeons, plastic surgeons, neurologists and others. *'75, 1446 pp. (7 x 10), 2074 il. (7 in full color), 6 tables, $132.50*

REHABILITATION OF THE FACIALLY DISFIGURED: Prevention of Irreversible Psychic Trauma by Early Reconstruction *by* **J. J. Longacre**, *Univ. of Cincinnati, Cincinnati. (2 Contributors)* The author emphasizes the importance of early definitive care and early reconstruction of the maimed and mutilated. Congenital deformities, malignancies and accidents are all covered. *'73, 144 pp. (7 x 10), 384 il., 2 tables, $14.75*

THE SYSTEMIC MANIFESTATIONS OF INFLAMMATORY BOWEL DISEASE *edited by* **William M. Lukash** *and* **Raymond B. Johnson,** *both of the National Naval Medical Center, Bethesda, Maryland. (30 Contributors)* Current thoughts on the etiology and epidemiology of inflammatory bowel disease are reviewed in this book. Stressed are the numerous systemic manifestations of the disease including the intestinal complications of toxic megacolon, malignancy, extra-intestinal manifestations of liver disease, skin involvement, ocular complications, arthritis, metabolic-endocrine implications, hematologic sequelae and urological complications. By analyzing the pathological course of inflammatory bowel disease and the guidelines for proper diagnosis and treatment, this book will aid the physician in establishing earlier and more astute diagnoses and in instituting appropriate care. *'75, 368 pp., 92 il. (3 in color), 26 tables, $15.50*

COMMON DUCT STONES *by* **Frank Glenn**, *Cornell Univ. Medical College, Ithaca, New York.* Surgeons and internists who diagnose, manage and treat biliary tract disease will find this book valuable. The first section is devoted to the history of biliary tract disease and its recognition and the development of surgical procedures in its treatment. The sequelae of the disease, cholelithiasis, choledocholithiasis and liver disease are also discussed. Equipment is described that enables the performance of operative cholangiography before removal of the gallbladder. A discussion is provided of the reported successes and failures using solvents and instruments in removing retained calculi. Circumstances that may favor allowing demonstrated retained common duct calculi to remain unmolested are discussed as well. Developments in the diagnosis of biliary tract disease since Röntgen introduced the use of x-rays are reviewed. *'74, 148 pp., 22 il., 5 tables, $11.50*

INTERNATIONAL SYMPOSIUM ON MALIGNANT HYPERTHERMIA *edited by* **R. A. Gordon, Beverley A. Britt** *and* **Werner Kalow**, *all of the Univ. of Toronto, Toronto, Canada. (66 Contributors)* This volume presents discussions of the clinical recognition and management of this highly fatal disorder, recognizes hereditary and genetic basis of the trait and reports basic investigations of the mechanisms involved. *'73, 512 pp., 131 il., 55 tables, $22.50*

Orders with remittance sent by air, postpaid

301-327 East Lawrence Avenue • Springfield • Illinois • 62717 • USA

BOC Roberts Venous Flow Stimulator tackles the problem of d.v.t. where it starts

Every patient undergoing surgery is at risk from deep vein thrombosis. According to the Registrar General's reports, the incidence of death from d.v.t. – induced post-operative pulmonary embolism, is steeply rising.

It has been demonstrated* that the occurrence of deep vein thrombosis can be dramatically reduced by the application of intermittent calf compression per-operatively to prevent venous stasis. This procedure is, however, successful only when the pressure cycle conforms to blood flow dynamics. Critical considerations are:

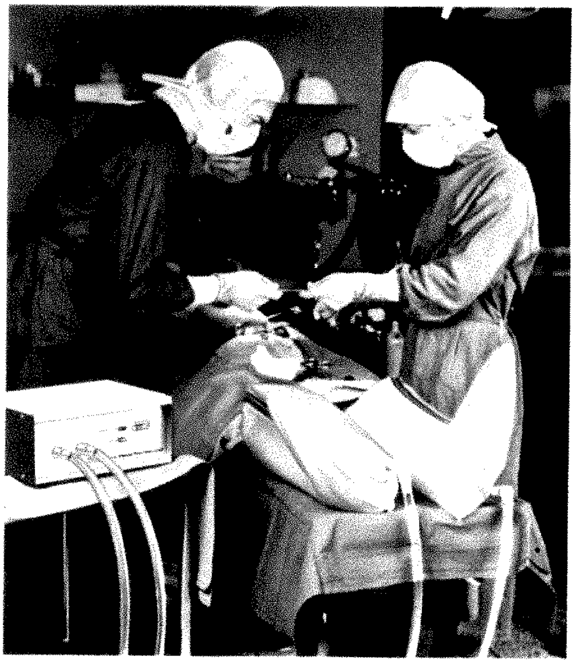
- The duration and magnitude of the applied pressure.
- The timing of the pressure cycle to give vessels the optimum time to refill between compression phases.

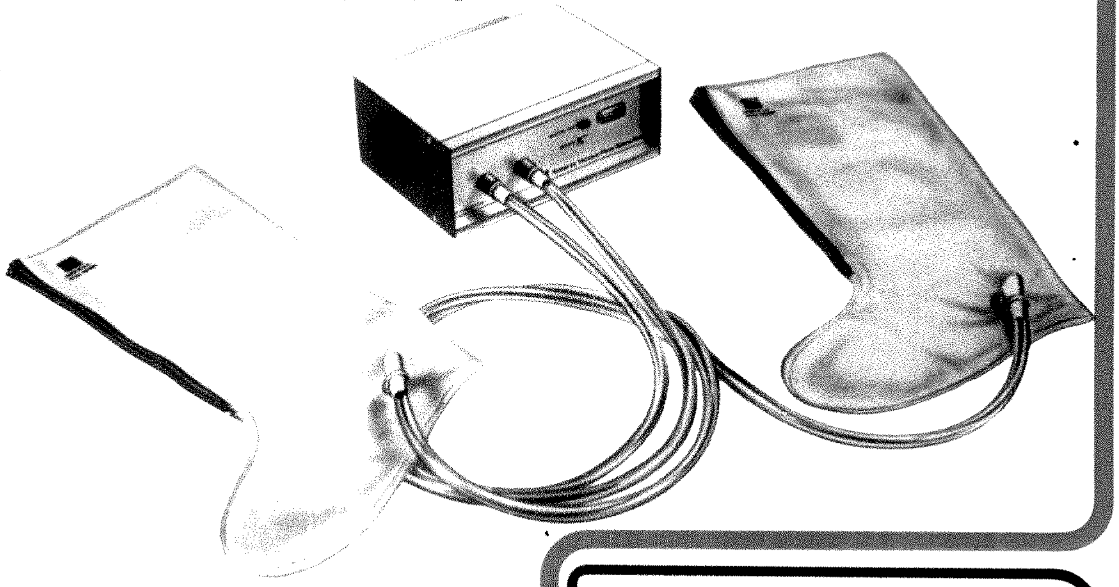
Only the BOC Roberts Venous Flow Stimulator meets these criteria precisely and automatically. Clinical trials indicate that the apparatus can eliminate over 75% of cases of post-operative d.v.t. without the need for chemical intervention.

If you would like to know more about this equipment, please write or telephone us at the address below.

*Roberts VC and [illegible]

BOC is here for life





BOC
Medishield

BOC Medishield
Elizabeth Way, Harlow,
Essex CM19 5AF England
Telephone Harlow [illegible]
Cables Brit[illegible]
Telex 814[illegible]

☐ Please send me details of the BOC Roberts Venous Flow Stimulator.
Name ....
Position ....
Hospital ....
Address ....
....
BJS

A new concept in surgical lighting
the DAYSTAR
major surgical light

Made in England by

DRAYTON CASTLE
SYBRON CORPORATION

Light Quality The **Daystar** provides cool shadow free colour corrected light giving maximum illumination and minimum heat in the surgical field.

An infinitely variable intensity controller means that you can regulate the level of light to suit your own requirements.

Positioning The **Daystar's** unrivalled ease of mobility puts the light where you want it and keeps it there without drift.

A snap-on autoclavable handle is provided to allow final surgical alignment where necessary.

Supplementary lights
An optional **Orbiter** attachment is available complete with its own intensity controller.

Track lights If you prefer track lighting the **Twinstar** combines **Daystar** quality light with twin track configuration.

Further information
Please complete and return the coupon for further details:

Please provide further details of the Daystar range of surgical lights by: (tick box)

Name ______________________

Position ______________________

Address ______________________

____

Tel. No. ______________________

Leaflet ☐

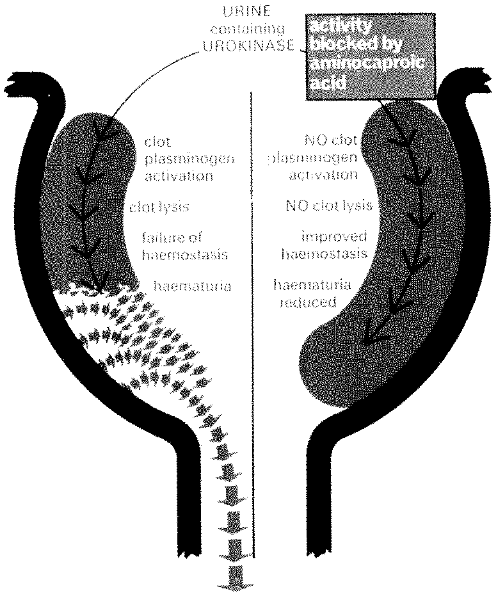
Representative ☐

Quotation ☐

Drayton Castle Limited,
Bridge Works, Bentinck Road, West Drayton,
Middlesex. Telephone: West Drayton 43741

P.J.S.9-75

The mechanism of post-prostatectomy bleeding and EPSIKAPRON® control



Epsikapron (aminocaproic acid) is rapidly excreted in the urine in high concentration ; there it inhibits urokinase, the fibrinolytic enzyme in urine. With the haemorrhage-sustaining property of urine blocked, the haemostatic coagulum becomes adequate, and blood loss is diminished substantially.

Epsikapron makes your prostatectomy patient's post-operative course smoother by diminishing :

the need for post-operative blood transfusion
clot retention
catheterization
the risk of infection
the period of hospitalization

Presentation

Epsikapron Solution for Injection 0.4 g/ml Box of 6 ampoules of 10 ml, each containing 4.0g aminocaproic acid (0022/5003) Epsikapron Effervescent Powder 50% Box of 30 sachets, each containing 3.0g aminocaproic acid (0022/5004) Epsikapron Syrup 0.3g/ml Bottle of 250ml (0022/5005)

EPSIKAPRON®

KabiVitrum

KabiVitrum Limited,
Bilton House,
Uxbridge Road,
London W5 2TH
Telephone: 01-567 4717 01-579 1871

The British Journal of Surgery

Vol. 62 : No. 9 : September 1975

Br. J. Surg. Vol. 62 (1975) 673–682

Whither thyrotoxicosis?

W. MICHIE*

SUMMARY

For 30 years the thyrotoxic patient has been subjected to a plurality of treatments by surgery, radio-iodine and long term anti-thyroid drugs. These therapies have been accepted as complementary to the needs of the individual patient, without regard for long term results or the economic situation as it affects both patient and hospital services. In the context of surgical treatment which is now available, it is suggested that the advantages of operation over other therapies presage a reversion to surgery as the treatment of choice.

It was in the autumn of 1905 that Dr Hector Mackenzie, a physician of St Thomas's Hospital, wrote of the treatment of thyrotoxicosis, that when for a particular disease there were several remedies, none of these remedies would prove to be particularly efficacious. To this oft-quoted aphorism might be added another, that when the aetiology of a disease remains obscure, therapy may prove to be empirical, is liable to be uncertain and is unlikely to be convincing. Current thinking involves immunological and metabolic mechanisms. The former may be humoral from deposition of immunoglobulins on the basement membrane of the thyroid follicular cell (Werner et al., 1972) or cellular from defective lymphocytic immune surveillance (Volpé et al., 1972).

Metabolic factors have implicated thyroid autoregulation of iodine, both in excess and depletion, with consequent inability to modulate thyroid function and activity (Ingbar, 1972), and in this respect thyrotoxicosis has been ascribed to defective control of thyroid hormone synthesis with abnormal regulation of the relative proportions of T_3 and T_4. Practical evidence of the metabolic thesis was a more than twofold increase in the incidence of thyrotoxicosis in Tasmania following the addition of potassium iodate to bread as prophylaxis against endemic goitre (Connolly et al., 1970).

Modalities of treatment

Currently the thyrotoxic patient is treated by destructive therapy by radio-iodine or surgery or by long term surveillance on anti-thyroid drugs in the hope of eventual remission. Each method has its advantages, disadvantages and complications.

Anti-thyroid drug therapy

There is much to commend the concept of long term anti-thyroid drug treatment and the desire to protect from destructive therapy patients who might achieve spontaneous euthyroidism. In practice many difficulties are encountered. Anti-thyroid drugs do not interfere with the fundamental nature of the disease process (Furth et al., 1966), but merely inhibit the synthesis and release of thyroid hormones. Early relapse occurs in more than half the patients when drug therapy is withdrawn (Hershman et al., 1966), and in others relapse follows over the course of several years. The initial hope that successful remission might be predictable on the basis of suppression of radio-iodine uptake by tri-iodothyronine (Alexander et al., 1966) has not materialized (Lowry et al., 1971), and presently no method exists whereby remission can be foretold for the individual patient.

As a practical proposition, general acceptance of long term anti-thyroid drug therapy would prove to be a mammoth task. The incidence of thyrotoxicosis is not less than 1 per 5000 of the population annually (Furszyfer et al., 1970), equivalent to 10 000–11 000 new patients per year in the United Kingdom. On the assumption that a patient on long term therapy should be seen monthly for the first 3 months and 3-monthly thereafter, there would be 60 000 attendances at thyroid clinics in the first year, and with next year's accumulating harvest 100 000 attendances in the second year, and so on. While accepting that long term anti-thyroid drug therapy should be evaluated, there are grounds for regarding the evaluation as a reasearch programme for the well-staffed university department. Its universal adoption would leave room for doubt, for over 90 per cent of the clinical work in the United Kingdom is carried out in district hospitals which do not have the staff, medical or technical, to sustain a programme of this nature.

Thyrotoxicosis is in essence a disease of exacerbation and remission, and lifelong supervision becomes essential, for patients do tend to default from a programme which by its nature must have continuing review for many years. An undoubted risk is thyrocardiac disability in the late fifties and sixties, and most physicians must be familiar with the elderly patient whose fibrillation does not respond to digitalis therapy.

---

* Aberdeen Royal Infirmary.

Radio-iodine therapy

Radio-iodine therapy has undoubted appeal. It is inexpensive and easy to administer, and the initial fear of neoplastic degeneration has not materialized (Saenger et al., 1968), though doubts have been expressed on possible long term effects in children (Starr et al., 1964). Genetic defects have not become apparent (Hayek et al., 1970), though gene mutation, being recessive, is not expressed in the first generation and must await the verdict of several generations.

Radio-iodine exerts its effect by interference with the replicative mechanism of the thyroid follicular cell (Greig, 1965), with the implication that the end point may be hypothyroidism in all patients if followed for sufficient length of time. The rate of interference is unpredictable, and therein lies the dual problem of slow rate of thyroid control and the progressive risk of thyroid failure. In general, however, the incidence of hypothyroidism increases *pari passu* with the dose of radio-iodine administered, and even with conventional doses hypothyroid rates of 80 per cent are quoted after 15 years (Greig, 1973). The hope that low energy, short range radiation from ^{125}I (Greig et al., 1970) would diminish interference with the nucleus of the thyroid follicular cell has not been fulfilled. Hypothyroid rates are similar to those following ^{131}I therapy (McDougall et al., 1971; Bremner et al., 1973).

Irrespective of the isotope used and the dosage régime adopted, a progressive and relentless hypothyroidism would seem inevitable. This is not without hazard. Overt hypothyroidism can readily be detected by routine tests of thyroid function, but forms less clinically obvious exist whose detection rests upon the evidence of clinical improvement from thyroxine administration or from the use of more sophisticated techniques (Hedley et al., 1971a; Evered et al., 1975). The number of patients treated each year may remain relatively constant, but the total number accumulates and becomes part of an increasing clinical burden. This can in large measure be solved by the adoption of an annual follow-up programme controlled by a computer-based register such as now operates in the major centres of Scotland (Hedley et al., 1970a). Without such help hazards continue. For the younger patient with persisting hypothyroidism there is a risk of developing ischaemic heart disease (Bastenie et al., 1971), and for old people who tend to forget their medicaments there is the risk of morbidity from hypothermia.

Thyroidectomy

Thyroidectomy also has its complications, some of which derive from the surgical procedure and others develop during postoperative follow-up. For some both potential risk and incidence have been overemphasized in the past; for others potential hazards have not received sufficient emphasis in the current literature.

Mortality

The mortality is negligible and may be nil in established thyroid clinics. In a personal series of 1500 thyrotoxic patients 1 death was attributable to surgery. This patient had anaesthetic complications during operation, following which she became decerebrate and died several months later.

Wound infection

Wound infection rarely occurs, presumably by reason of hyperdynamic circulation and increased vascularity in the operation area.

Wound haemorrhage

With reasonable care wound haemorrhage should be negligible. It may be present in either of two locations: above or below the strap muscles. The former is more frequently seen and can be circumvented if bleeding from the anterior jugular plexus of veins is avoided. The latter is rarely seen but is potentially dangerous. It derives from inadequate ligature of a major vessel in one of the lobes; the haematoma develops rapidly, lies laterally in the neck and must be evacuated quickly.

Nerve injuries

Potential injuries are several, and taken in chronological order of occurrence at operation four nerves are at risk.

Cutaneous nerves may be avoided by careful raising of the upper skin flap, when the nerve may be seen lying immediately deep to platysma. Section is followed by loss of sensation under the chin, which becomes a matter of inconvenience to the shaving male.

Superior laryngeal nerve: Of the nerves which may be involved in thyroid surgery, the superior laryngeal nerve is most at risk, though the danger remains the least publicized. It stems from the vagus below the ganglion nodosum, descends in company with the superior thyroid artery and soon divides into internal and external branches. The larger internal branch pierces the thyrohyoid membrane and supplies motor fibres to the intrinsic muscles of the larynx and mucosal sensation above vocal cord level. The external is of fine calibre and proceeds in medial proximity to the superior thyroid artery to supply the cricothyroid muscle. Though normally it lies outwith the cervical fascial investment of the superior pole, it may in 20 per cent of patients pass between the branches of the superior thyroid artery as they disperse on the superior pole (Moosman and De Weese, 1968). Interference with the cricothyroid muscle or its innervation decreases vocal cord tension. The voice becomes harsh, loses volume and pitch and tires easily. On laryngoscopy the cord becomes crenated and thickened and an ivory hue replaces normal pearly whiteness. Cord movement remains unimpaired.

The internal branch is at risk where traction is employed to bring down an enlarged superior pole which lodges behind the larynx. When the entire superior laryngeal nerve is involved, swallowing, particularly of fluids, is additionally disturbed (Hirzel, 1958). Fluids seep into the larynx by day and saliva at night. Persisting coughing and spluttering ensue and pneumonitis may supervene. The patient gradually adopts trick drinking habits by holding the chin forward and tilting the head to one side. By reason of its more fortunate anatomical location, internal laryngeal nerve involvement is comparatively rare, but voice changes from external laryngeal nerve interference may occur in varying degree in 20 per cent or more of patients.

Cervical sympathetic chain: Damage to the cervical sympathetic chain is not infrequent in malignant goitres, but is one of the rarer complications of thyroidectomy for thyrotoxicosis. The author has seen this in 2 patients. Injury occurs during ligation of the inferior thyroid artery, and myosis, ptosis and enophthalmos ensue. Though the lesion is described as Horner's syndrome, the vascular symptoms which form part of this syndrome are generally absent (Smith and Murley, 1965). It may be that the autonomic fibres subserving facial sweating synapse more proximally than do those from the superior cervical ganglion, which pass via the internal carotid artery plexus to the ophthalmic division of the trigeminal and the nasociliary nerves to supply the dilator pupillae muscle.

Recurrent laryngeal nerve: Injury is widely publicized, and has a recorded incidence which varies from 3·9 per cent of the nerves exposed to risk (Gisselsson, 1949) to nil (Wade, 1961). In the author's series permanent paresis was less than 0·5 per cent of the nerves at risk. It is more often seen in thyroidectomy for non-toxic goitre when the nerve may be displaced laterally from the trachea and oesophagus by colloid cyst intrusion. Routine exposure is believed by some to reduce the incidence of nerve injury (Lahey, 1938; Riddell, 1970), though this is not universal practice (Michie, 1970). Paresis is frequently temporary and may develop postoperatively, but if a trusted anaesthetist has recorded vocal cord movement by direct laryngoscopy at the end of the operation it can be assumed that full recovery will eventuate.

The results of nerve suture carried out at the time of initial operation or by a subsequent procedure are considered satisfactory by some (Siribodhi et al., 1963; Doyle et al., 1967), but inadequate by others (Lahey, 1944; Murakami and Kinchner, 1971), principally by reason of axonal confusion in the regenerating nerve with random re-innervation of antagonistic adductor and abductor laryngeal musculature (Boles and Fritzell, 1969).

Bilateral nerve injury, though extremely rare in thyroid clinics, is a catastrophe. Tracheostomy must follow its detection and must be maintained until laryngeal function can be restored by procedures designed to re-establish the glottic aperture. This may be achieved by arytaenoidopexy or arytaenoidectomy. In the former the arytaenoid cartilage is mobilized submucously via an external approach through the inferior constrictor muscle and maintained in a lateral position by suture to the omohyoid (King and Gregg, 1948). In the latter the arytaenoid is resected submucously by endoscopic procedure (Thornell, 1950).

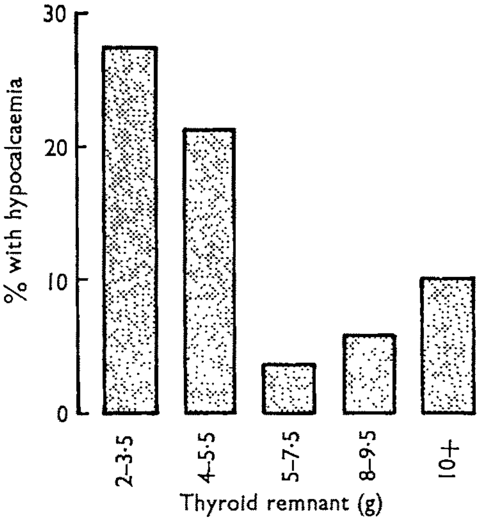


Fig. 1. Change of risk of postoperative transient hypocalcaemia with estimated size of remnant after partial thyroidectomy. (Reproduced from Michie, 1970.)

Hypocalcaemia

The hypothesis that parathyroid damage or infarction explains the hypocalcaemic and tetanic manifestations which occasionally follow thyroidectomy for thyrotoxicosis is widely acclaimed (Lachmann, 1941; Davis et al., 1961; Riddell, 1962), but cannot be accepted on present clinical, biochemical and experimental evidence. Graves' disease, particularly untreated and of prolonged duration, induces gross skeletal decalcification (von Recklinghausen, 1891). Thyroid hormones act on the bone cell, accelerating turnover rate, with increasing calcium loss in the urine and faeces, and culminating in a state of hungry bones. When partial thyroidectomy is performed leaving substantial remnants, the risk of hypocalcaemia is minimal, but after radical thyroidectomy, particularly in the young florid thyrotoxic with active bone metabolism, the risk is greatly enhanced (*Fig.* 1).

Hypocalcaemic symptoms appear within a few hours of operation and are likely to persist until the negative calcium balance has been corrected by adequate calcium supplement (Michie et al., 1971). When the calcium balance has been restored, and the bones are no longer hungry, hypocalcaemic manifestations of paraesthesia and tetany disappear and calcium homeostasis is maintained without further supplement. This sequence of events cannot be explained on the basis of damage to the parathyroids or their blood supply. When total thyroparathyroidectomy is performed, as may happen in laryngopharyngectomy, hypocalcaemic

Table I: REPORTED INCIDENCE OF HYPOTHYROIDISM FOLLOWING THYROIDECTOMY FOR THYROTOXICOSIS

Author	Incidence of hypothyroidism (%)
Pemberton (1930)	2·9
Riddell (1961)	3·3
Cattell (1949)	4·5
Bartels (1952)	7·3
Murley and Rigg (1968)	7·5
Taylor and Painter (1962)	9·3
Goadby (1937)	18·0
Thomson et al. (1930)	19·5
Hershman (1966)	29·7
Hedley et al. (1970b)	35·6
Cassidy (1962)	38·0
Nofal et al. (1966)	42·0
Beahrs and Sakulsky (1968)	48·0

Table II: INCIDENCE OF HYPOTHYROIDISM IN RELATION TO TOTAL GLAND MASS

Gland weight (g):	Hypothyroid rate (%):
10–29	42
30–49	51
50–69	46
70–99	31
>100	35

manifestations are delayed until 48–60 hours after operation; in contrast, significant hypocalcaemic symptoms which follow thyroidectomy for thyrotoxicosis are apparent within a few hours and invariably within 24 hours of operation. Furthermore, hypocalcaemia is extremely rare (Murley and Peters, 1961) or may not be seen (Michie et al., 1971) after thyroidectomy for non-toxic goitre, even where resection has been severe.

Experimentally, two or more parathyroids can be removed without hypocalcaemic symptoms (Welsh, 1898; Sanderson et al., 1960), and though the parathyroids are known to be at risk in thyroid surgery (Murley and Peters, 1961), interference sufficient to produce hypocalcaemia would seem improbable. Further supportive evidence comes from the surgery of parathyroid adenoma. Accepted surgical policy in many centres is to identify each of the remaining parathyroids histologically, and since adequate biopsy entails removal of approximately half the gland, the patient is left with the equivalent of one and a half parathyroids. Despite this, and excluding parathyroid tumours associated with osteitis fibrosa cystica, abnormal serum calcium values following operation are unusual.

Available evidence would therefore suggest that the term 'postoperative hypoparathyroidism' with its implication of parathyroid damage or interference is misleading and without factual evidence, and that it should be discarded in favour of 'postoperative hypocalcaemia', which is largely self-rectifying when calcium balance is restored.

Recurrent thyrotoxicosis

Provided that adequate thyroidectomy has been performed, the recurrence rate is around 6 per cent (Hedley et al., 1970b), and recurrence may be seen at any stage in the life of the postoperative thyrotoxic patient. It usually appears in the early postoperative years, and failure to achieve euthyroidism after operation is not unknown and has occurred twice in the author's series. On the other hand, recurrence may be delayed for 20 years or more after surgery.

The mechanism of recurrent thyrotoxicosis is unknown but continuing failure of T_3 suppression of ^{131}I uptake suggests the presence of an extrapituitary stimulator. In a retrospective study of patients treated by subtotal thyroidectomy between 2 and 21 years previously (Hedley et al., 1971b), 83 per cent showed complete suppression while none of the patients with recurrent thyrotoxicosis suppressed. In a recent study (Mukhtar et al., 1975) thyroid-stimulating immunoglobulins were detected in the serum of all patients with untreated Graves' disease and following operation were found to disappear in 83 per cent and persist in 17 per cent, a figure identical with the number of patients who failed to suppress (Hedley et al., 1971b). These results suggest that thyroid-stimulating immunoglobulins may play a role in the pathogenesis of recurrent thyrotoxicosis.

Recurrent thyrotoxicosis responds to radio-iodine but not to further surgery. In one recorded series 10 out of 10 patients (McLarty et al., 1969) and in another 5 out of 6 patients (Hedley et al., 1970b) had further recurrence after two or more thyroidectomies.

Hypothyroidism

Without doubt hypothyroidism is the major complication of thyroidectomy for thyrotoxicosis. The recorded incidence (*Table I*) has varied from 2·9 per cent (Pemberton, 1930) to 48 per cent (Beahrs and Sakulsky, 1968). The higher figures have, by and large, been recorded in the past 10–15 years, and probably represent an increased awareness of the clinical problem and a more critical evaluation of postoperative thyroid status. Historical evidence from the turn of the century suggests that the higher figures may be more realistic (Williamson, 1896; Mackenzie, 1905; Sattler, 1908; Campbell, 1921). Approximately 20 per cent of untreated patients died acutely in crisis, while 40 per cent pursued a chronic course of exacerbation and remission into thyrocardiac disability. Some 30–40 per cent ultimately improved spontaneously, and while some remained euthyroid, others lapsed into hypothyroidism over the course of several years (Baldwin, 1895; Campbell-Gowan, 1895; Sattler, 1908). It would appear, therefore, that in some thyrotoxic patients there is a naturally progressive thyroid impairment leading to decreased reserves of thyroid function or frank failure, and it may be that in these patients surgery merely accelerates the natural course of the disease, compressing the events of many years into a matter of weeks or a few months.

In an attempt to define the factors responsible for hypothyroidism, we made a study of thyrotoxic patients operated upon during the years 1965–72 (Michie et al., 1972; Pegg et al., 1973). The factors examined were in preoperative preparation, surgical management and postoperative behaviour. It became clear that several factors did not influence postoperative thyroid status. The duration of anti-thyroid drug therapy varied from 4 weeks to several years, as determined by the physicians who supervised the preoperative care of the patient. No correlation was found between postoperative hypothyroidism and the duration of therapy, or the amount of anti-thyroid drugs prescribed. Despite considerable variation in the size of the glands (*Table II*), no relationship between total gland mass and hypothyroidism could be demonstrated. It is generally accepted that higher anti-cytoplasmic (but not anti-thyroglobulin) antibody responses indicate an increased risk of postoperative hypothyroidism (Irvine et al., 1962; Van Welsum et al., 1974); formerly we were unable to confirm this, but in recent years we have found that as the titre of anticytoplasmic antibody increased from negative to strongly positive, the number of euthyroid patients decreased by an additional 14 per cent ($P<0{\cdot}001$) and anti-thyroglobulin antibody by 4 per cent ($P<0{\cdot}01$). Even so, though the trend is marked, the relative size of the association remains small.

The significance factor which determined the behaviour of a group of patients after partial thyroidectomy was the size of the thyroid remnant left at operation (*Table III*). Remnants of less than 4 g carried the highest hypothyroid rate, whereas those of 10 g or more carried the lowest ($P<0{\cdot}001$). It must be emphasized, however, that size alone is not the only criterion, for with a remnant of 4 g or less there was a 36 per cent incidence of euthyroidism, while with a remnant of 10 g or more hypothyroidism occurred in 19 per cent of patients.

When remnant weights are charted against percentage hypothyroidism, there would appear to be two relevant indices. Hypothyroidism decreased by about 10 per cent/g as remnant weight increased to 7·5 g, and there was a similar fall thereafter of 2 per cent/g as remnants increased to 16 g (*Fig.* 2). Exponential interpretation of this graph would suggest that there is a group of patients, comprising some 15 per cent, who might develop hypothyroidism irrespective of remnant size. It would seem possible that the patients in this group are precisely the thyrotoxic patients who at the turn of the century were capable of achieving euthyroidism and later hypothyroidism without any form of therapy.

The surgeon, like his counterpart the physician in nuclear medicine, must therefore accept a measure of post-treatment hypothyroidism, and for the surgeon this figure is unlikely to be less than 25 per cent (*Table IV*). Whichever the method of treatment, there is a clinical and ethical responsibility for the continuing supervision of these patients. It was the author's practice to estimate protein-bound ^{127}I levels at 1 and 4 months after operation, and yearly thereafter, until the services of a computer-assisted register came into operation (Hedley et al., 1970a). From a study of these patients a distinctive pattern has emerged (*Table V*). Where both the 1-month and 4-month levels are below 4 μg per cent the incidence of hypothyroidism is 77 per cent. Where one of the values is below 4 μg per cent the incidence of hypothyroidism is around 20 per cent, but a rising value holds a more favourable prognosis than a falling one. Where both levels are above 4 μg per cent all the patients are euthyroid, and the risk of developing hypothyroidism subsequently is negligible.

The definition of postoperative hypothyroidism at an early date is in accord with the experience of others (Olsen et al., 1970; Caswell and Maier, 1972), and may suggest that when a rising incidence is recorded over several years (Nofal et al., 1966; Gough and Neill, 1974), a lower index of clinical suspicion of

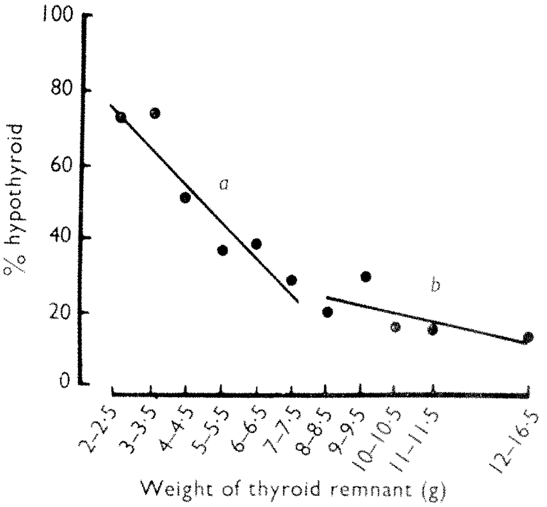


Fig. 2. Hypothyroidism in relation to size of thyroid remnant. *a*, 2–7·5 g: slope 9·6 per cent/g; *b*, 8–16·5 g: slope 2·1 per cent/g.

Table III: INCIDENCE OF HYPOTHYROIDISM IN RELATION TO MEAN ESTIMATED REMNANT WEIGHT

Remnant weight (g):	Hypothyroid rate (%):
2·4	64
5–7	39
8–10	25
>10	19

Table IV: INCIDENCE OF HYPOTHYROIDISM IN RELATION TO MEAN ESTIMATED REMNANT WEIGHT FOR EACH YEAR FROM 1965 TO 1972

Year	Mean estimated remnant weight (g)	Hypothyroid rate (%)
1965	3·3	63
1966	3·8	73
1967	5·1	43
1968	8·0	36
1969	7·8	26
1970	7·6	27
1971	6·5	25
1972	8·1	25

Table V: INCIDENCE OF HYPOTHYROIDISM IN RELATION TO PROTEIN-BOUND ^{127}I LEVELS AT 1 AND 4 MONTHS AFTER OPERATION

Protein-bound ^{127}I (μg %)		Hypothyroid rate (%)
1 mth	4 mth	
<4	<4	77
≥4	<4	35
<4	≥4	5
≥4	≥4	0

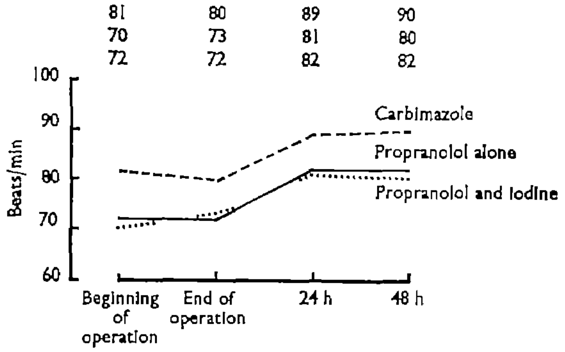


Fig. 3. Mean pulse rates in thyrotoxic patients undergoing partial thyroidectomy. (Reproduced from Michie et al., 1974.)

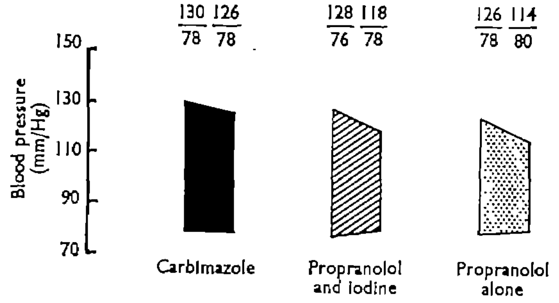


Fig. 4. Mean blood pressure at the beginning and end of operation in thyrotoxic patients undergoing partial thyroidectomy. (Reproduced from Michie et al., 1974.)

Table VI: PREPARATION OF THE THYROTOXIC PATIENT FOR SURGERY

Group	Treatment	No. of cases
1	Carbimazole and Lugol's iodine	42
	Carbimazole, propranolol and Lugol's iodine	69
2	Propranolol and Lugol's iodine	51
3	Propanolol alone	47

postoperative hypothyroidism may have been accepted during the first postoperative year.

Provided that a remnant of 8–9 g is left, postoperative thyrotoxic patients can be offered a group prediction of 70–75 per cent euthyroidism, and the status of the individual patient can with reasonable assurance be defined within a year. This is a matter of some importance for the busy surgeon for whom the facilities of a computer-assisted register may not be available. Although ideally all patients subjected to surgery merit lifelong supervision, the surgeon can concentrate his attention on the 25–30 per cent of patients whose early postoperative protein-bound ^{127}I levels have been less than 4 μg per cent. In this respect the surgeon is at an advantage over his medical colleague.

Beta-adrenergic blockade in thyrotoxicosis

Further advantages to the surgically treated patient may accrue from pretreatment by beta-adrenergic blockade. For many years the similarity between the clinical features of hyperthyroidism and increased sympathetic activity has been recognized. Sympathetic blockade is not a new concept. Early attempts were surgical, initially by section of the cervical sympathetic chain (Jaboulay, 1897), and later by adrenalectomy or adrenal denervation (Crile, 1929). There followed the use of several pharmacological agents to reduce sympathetic overactivity: reserpine (Buchanan et al., 1959), guanethidine (Waldstein et al., 1964) and alpha-methyldopa (Theilen et al., 1963). Later came the first beta-blocker, pronathalol, which was discarded because of adverse reactions (Wilson et al., 1964), but with the introduction of propranol, beta-blockade became a practical proposition (Rowlands et al., 1965; Turner et al., 1965). Initially, it was used in the treatment of thyrotoxic crisis and later as an adjuvant to radio-iodine therapy. More recently, propranol has been found of value in the surgical management of thyrotoxicosis (Lee et al., 1973; Michie et al., 1974).

It was in 1970 that we decided to investigate the use of propranolol in the surgery of thyrotoxicosis, and since then we have employed it, either alone or in combination with other drugs, in a series of patients. Our approach has been cautious, and initially we used it in combination with carbimazole and Lugol's iodine (iodine with potassium iodide), later replacing carbimazole with propranolol and finally using propranolol as the sole preoperative agent. Though these stages inevitably overlapped we were able to study the behaviour of patients prepared for operation with propranolol, both with and without Lugol's iodine, and to compare them with a similar group conventionally prepared with carbimazole and iodine. There were approximately 40–50 patients in each group (*Table VI*).

Pulse rate and blood pressure were monitored during hospitalization, and biochemical records of calcium, protein-bound ^{127}I, serum alkaline phosphatase and total protein were made when the patient was first seen, immediately before and after operation, and at 24 and 48 hours and at 1 and 4 months after operation.

Pulse rate was on average 10 beats per minute slower in the propranolol groups (*Fig.* 3). Blood pressure was similar in all the groups except that the mean systolic reading at the end of operation was 10 mm Hg lower in the propranolol patients (*Fig.* 4). Serum calcium corrected for serum protein levels (Dent, 1962) was the same when first seen but higher through operation in the propranolol groups, though these differences were not apparent at 1 and 4 months after operation (*Fig.* 5). In general, serum alkaline phosphatase levels showed a parallel reduction in the three groups, excepting the concentration at 1 month after operation, which was higher in the propranolol patients (*Fig.* 6). Both the serum calcium and serum alkaline phosphatase levels are in harmony with the thesis of a healing thyrotoxic, osteodystrophy occurring at a later phase in the propranolol groups.

Serum protein-bound ^{127}I values were the same at the initial examination but were significantly higher in propranolol-pretreated patients while they remained

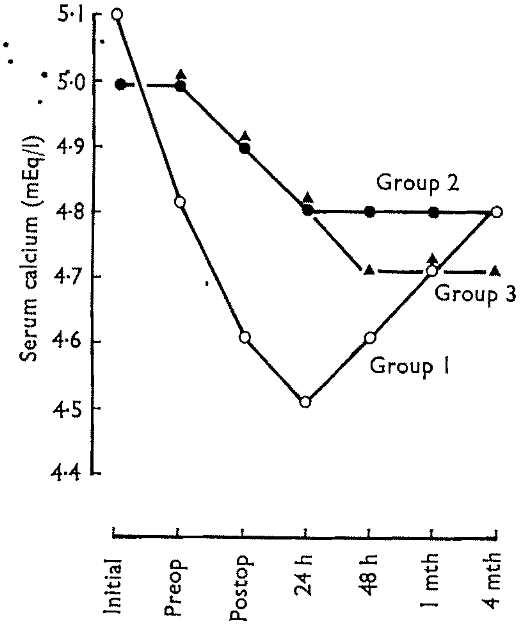


Fig. 5. Comparison of serum calcium values in relation to preoperative treatment. (Reproduced from Michie et al., 1974.)

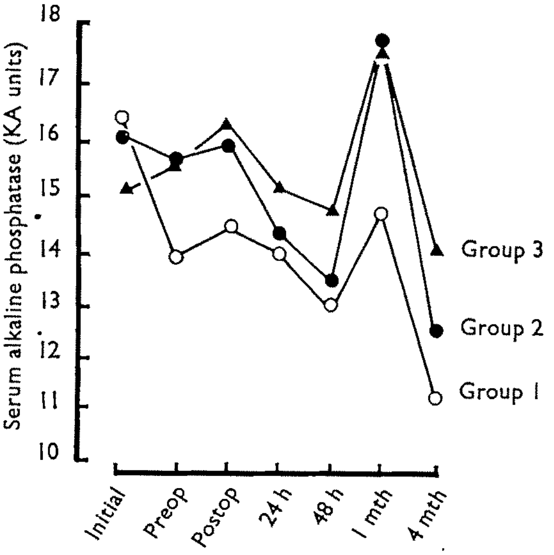


Fig. 6. Comparison of serum alkaline phosphatase values in relation to preoperative treatment. (Reproduced from Michie et al., 1974.)

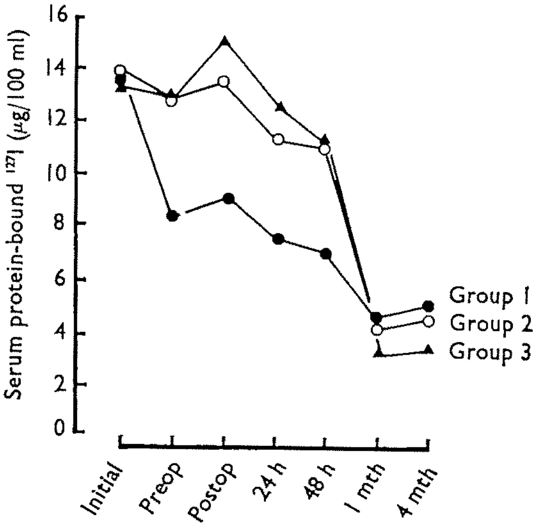


Fig. 7. Comparison of serum protein-bound ^{127}I values in relation to preoperative treatment. (Reproduced from Michie et al., 1974.)

Table VII: LEVELS OF SIGNIFICANCE OF PROTEIN-BOUND ^{127}I AT 1 AND 4 MONTHS AFTER OPERATION ACCORDING TO PREOPERATIVE THERAPY

Comparison	Time of protein-bound ^{127}I estimation 1 mth	4 mth
Carbimazole and iodine versus propranolol and iodine	Not significant	Not significant
Carbimazole and iodine versus propranolol	$P = 0{\cdot}005$	$P = 0{\cdot}005$
Propranolol and iodine versus propranolol	$P = 0{\cdot}02$	$P = 0{\cdot}005$

Table VIII: COMPARISON OF PATIENTS PREPARED FOR OPERATION WITH CARBIMAZOLE AND LUGOL'S IODINE, AND PROPRANOLOL WITH AND WITHOUT LUGOL'S IODINE

Treatment	Mean no. of outpatient attendances	Mean duration of treatment (d)
Carbimazole and Lugol's iodine	9	143
Propranolol and Lugol's iodine	4	46
Propranolol alone	3	25

in hospital (*Fig. 7*). By the seventh postoperative day the protein-bound ^{127}I levels had returned to normal, but fell considerably lower at 1 and 4 months after operation. The size of the decrease is most significant in the patients treated with propranolol alone (*Table VII*). The reason might be that with Lugol's solution, iodine is readily available for iodoprotein synthesis in the thyroid follicular cell, but a more likely explanation is that with propranolol alone, patients lack the stimulus which carbimazole and iodine give in promoting the resumption of thyrotropic control of thyroxine synthesis. In practical terms, while normal protein-bound ^{127}I values are possible at 1 and 4 months after operation in the carbimazole-prepared patient, the same may not be achieved until 12–15 months after operation and even longer with propranolol alone.

If a new form of therapy is to merit consideration it must offer significant advantages over current methods of treatment. This can be measured only in the wide context of a comparison of all three methods of treatment. Long term anti-thyroid drug therapy is labour-intensive and runs a potential risk of late recurrence with thyrocardiac damage. In the destructive therapies, either by radio-iodine or by surgery, the problem is that of hypothyroidism. Following radio-iodine, potential hypothyroidism in all patients cannot be gainsaid. Surgery, with 25–30 per cent hypothyroidism, might be regarded as the least bad bet, and though there is an ethical responsibility for continuing supervision, the fate of the remaining 70–75 per cent, recurrent thyrotoxicosis excluded, should be secure.

The aims of treatment should be to secure the best result, with maximum safety, at the least economic cost to patient and hospital, and with the greater convenience to the patient. We believe that the use of propranolol achieves these aims. The mean number of outpatient attendances and the duration of treatment for different preoperative therapies are detailed in *Table VIII*. Admittedly, the mean duration for carbimazole at 314 days includes patients who failed to achieve remission after several months' therapy, while in patients prepared with surgery in mind from the time of diagnosis the mean duration was 82 days. Equally, the present position is understated in that preoperative preparation with propranolol can be limited to 5–6 days, and admission to hospital for surgery to 3–4 days, so that the whole episode of treatment for thyrotoxic illness can be reduced to 10 days. Hence, when physician and surgeon jointly agree that for an individual patient surgery is the method of choice, the sooner it is completed, the better it is received by, and the better for, the patient. In these days of economic stringency when both husband and wife must strive to maintain home and family, it is a matter of no mean import that a hospital procedure be reduced to a minimum.

For the surgeon also there are advantages. The propranolol-prepared gland is more pliable and mobilizes easily. It is less friable and bleeds less. Thyroidectomy can be achieved with blood loss as small as 15–20 ml, and the technical dangers of surgery are thereby considerably reduced.

The use of propranolol without iodine is open to criticism on the grounds that the patient remains exposed to high circulating levels of thyroid hormones, and is thereby ill-equipped to respond to situations of stress such as bleeding or cardiac infarction during operation. Preoperative Lugol's iodine promotes the acute Wolff–Chaikoff effect of reduced thyroid hormone synthesis with changes similar to those produced by conventional anti-thyroid drugs (Wolff and Chaikoff, 1948). Though 1 patient recently did have a small cardiac infarct shortly after operation from which she made an uneventful recovery, our impression has been that in general the behaviour of patients prepared with propranolol, with or without Lugol's iodine, has not been different before, during or after operation from those prepared with carbimazole.

Beta-adrenergic blockade appears to be a safe procedure provided that certain rules are observed. It cannot be used in patients with obstructive airways disease or with a past history of asthma. It is ineffective when the patient is under treatment with antidepressant drugs such as Tryptizol. Dosage must be carefully observed, and if there is doubt about the patient's co-operation or reliability she should be admitted to hospital for preoperative therapy. In particular, the immediate preoperative dose must not be overlooked, for patients can quickly emerge from beta-blockade.

The advantages and disadvantages of treatment by different disciplines are difficult to define and quantify, but it may not be without significance that recent trends in the United States have revealed an increase in the percentage of patients with Graves' disease who have been treated surgically (Schlicke, 1974). This has been ascribed to growing disenchantment with conservative treatment. While the swing to radio-iodine therapy in the United Kingdom has never been so pronounced as in the United States, where choice of treatment may to greater degree be influenced by economic costs, it may be that in the next few years there will be an increasing advocacy of surgery for the thyrotoxic patient.

References

ALEXANDER W. D., HARDEN R. MCG. and SHIMMINS J. (1966) Thyroidal suppression by triiodothyronine as a guide to duration of treatment of thyrotoxicosis with antithyroid drugs. *Lancet* **2**, 1041–1044.

BALDWIN W. W. (1895) Graves' disease, succeeded by thyroid atrophy. *Lancet* **1**, 145–146.

BARTELS E. C. (1952) Hyperthyroidism: the evaluation of treatment with antithyroid drugs followed by subtotal thyroidectomy. *Ann. Intern. Med.* **37**, 1123–1134.

BASTENIE P. A., VANHAELST L., BONNYNS M., NEVE P. and STAQUET M. (1971) Preclinical hypothyroidism: a risk factor for coronary heart disease. *Lancet* **1**, 203–204.

BEAHRS O. H. and SAKULSKY S. B. (1968) Surgical thyroidectomy in the management of exophthalmic goiter. *Arch. Surg.* **96**, 512–516.

BOLES R. and FRITZELL B. (1969) Injury and repair of the recurrent laryngeal nerves in dogs. *Laryngoscope* **79**, 1405–1408.

BREMNER W. F., MCDOUGALL J. R. and GREIG W. R. (1973) Results of treating 297 thyrotoxic patients with ^{125}I. *Lancet* **2**, 281–282.

BUCHANAN J., BUCHANAN W. W., CROOKS J. and GALE G. E. (1959) The use of reserpine in the treatment of thyrotoxicosis. *Scott. Med. J.* **4**, 486–490.

CAMPBELL J. M. H. (1921) Some aspects of exophthalmic goitre. *Q. J. Med.* **15**, 55–68.

CAMPBELL-GOWAN B. (1895) Myxoedema and its relation to Graves' disease. *Lancet* **1**, 478–480.

CASSIDY C. E. (1962) The treatment for hyperthyroidism *Med. Clin. North Am.* **46**, 1201–1212.

CASWELL H. T. and MAIER W. P. (1972) Results of surgical treatment for hyperthyroidism. *Surg. Gynecol. Obstet.* **134**, 218–220.

CATTELL R. B. (1949) Surgical treatment of hyperthyroidism. *Clin. Endocrinol.* **9**, 999–1006.

CONNOLLY R. J., VIDOR G. I. and STEWART J. C. (1970) Increase in thyrotoxicosis in endemic goitre area after iodation of bread. *Lancet* **1**, 500–502.

CRILE G. (1929) Interdependence of thyroid, adrenals and nervous system. *Am. J. Surg.* **6**, 616–620.

DAVIS R. H., FOURMAN P. and SMITH J. W. G. (1961) Prevalence of parathyroid insufficiency after thyroidectomy. *Lancet* **2**, 1432–1435.

DENT C. E. (1962) Some problems of hyperparathyroidism. *Br. Med. J.* **2**, 1419–1425.

DOYLE P. J., BRUMMETT R. E. and EVERTS E. C. (1967) Results of surgical section and repair of the recurrent laryngeal nerve. *Laryngoscope* **77**, 1245–1254.

EVERED D., YOUNG E. T., TUNBRIDGE W. M. G., ORMSTON B. J., GREEN E., PETERSEN V. B. and DICKENSON P. H. (1975) Thyroid function after subtotal thyroidectomy for hyperthyroidism. *Br. Med. J.* **1**, 25–27.

FURSZYFER J., KURLAND L. T., MCCONAHEY W. M. and ELVEBACK L. R. (1970) Graves' disease in Olmsted County, Minnesota: 1935 through 1967. *Proc. Staff Meet. Mayo Clin.* **45**, 636–644.

FURTH E. D., RIVES K. and BECKER D. V. (1966) Non-thyroidal action of propylthiouracil in euthyroid, hypothyroid and hyperthyroid man. *Clin. Endocrinol.* **26**, 239–246.

GISSELSSON L. (1949) Laryngeal paralysis following thyroidectomy. *Acta Chir. Scand.* **99**, 154–162.

GOADBY H. K. (1937) Results of surgical treatment in series of cases of Graves' disease. *St Thomas's Hosp. Rep.* **2**, 77–90.

GOUGH A. L. and NEILL R. W. (1974) Partial thyroidectomy for thyrotoxicosis. *Br. J. Surg.* **61**, 939–942.

GREIG W. R. (1965) Radiation, thyroid cells and ^{131}I therapy: a hypothesis. *Clin. Endocrinol.* **25**, 1411–1417.

GREIG W. R. (1973) Radioactive iodine therapy for thyrotoxicosis. *Br. J. Surg.* **60**, 758–765.

GREIG W. R., SMITH J. F. B., ORR J. S. and FOSTER C. J. (1970) Comparative survivals of rat thyroid cells *in vivo* after ^{131}I, ^{125}I and X-irradiations. *Br. J. Radiol.* **43**, 542–548.

HAYEK A., CHAPMAN E. M. and CRAWFORD J. D. (1970) Long-term results of treatment of thyrotoxicosis in children and adolescents with radioactive iodine. *New Engl. J. Med.* **283**, 949–953.

HEDLEY A. J., FLEMMING C. J., CHESTERS M. I., MICHIE W. and CROOKS J. (1970b) Surgical treatment of thyrotoxicosis. *Br. Med. J.* **1**, 519–523.

HEDLEY A. J., HALL R., AMOS J., MICHIE W. and CROOKS J. (1971a) Serum-thyrotropin levels after subtotal thyroidectomy for Graves' disease. *Lancet* **1**, 455–458.

HEDLEY A. J., ROSS I. P., BECK J. S., DONALD D., ALBERT-RECHT F., MICHIE W. and CROOKS J. (1971b) Recurrent thyrotoxicosis after subtotal thyroidectomy. *Br. J. Surg.* **4**, 258–261.

HEDLEY A. J., SCOTT A. M., WEIR R. D. and CROOKS J. (1970a) Computer-assisted follow-up register for the north-east of Scotland. *Br. Med. J.* **1**, 556–558.

HERSHMAN J. M. (1966) The treatment of hyperthyroidism. *Ann. Intern. Med.* **64**, 1306–1314.

HERSHMAN J. M., GIVENS J. R., CASSIDY C. E. and ASTWOOD E. B. (1966) Long-term outcome of hyperthyroidism treated with antithyroid drugs. *Clin. Endocrinol.* **26**, 803–807.

HIRZEL L. F. (1958) The superior laryngeal nerve in relation to thyroid surgery. *West. J. Surg.* **66**, 322.

INGBAR S. H. (1972) Autoregulation of the thyroid: response to iodine excess and depletion. *Proc. Staff Meet. Mayo Clin.* **47**, 814–823.

IRVINE W. J., MACGREGOR A. G. and STEWART A. E. (1962) The prognostic significance of thyroid antibodies in the management of thyrotoxicosis. *Lancet* **2**, 843–847.

JABOULAY M. cited by PONCET M. A. (1897) Le traitement chirurgical du goître exophthalmique par la section ou la résection du sympathique cervical. *Bull. Acad. Méd.* **38**, 121–125.

KING B. T. and GREGG R. L. (1948) Anatomical reason for various behaviour of paralyzed vocal cords. *Oto. Rhin. Laryngol.* **57**, 925–944.

LACHMANN A. (1941) Hypoparathyroidism in Denmark. *Acta Med. Scand.* (*Suppl.* 121) 1–269.

LAHEY F. H. (1938) Routine dissection and demonstration of recurrent laryngeal nerve in subtotal thyroidectomy. *Surg. Gynecol. Obstet.* **66**, 775–777.

LAHEY F. H. (1944) Exposure of recurrent laryngeal nerves in thyroid operations: further experiences. *Surg. Gynecol. Obstet.* **78**, 239–244.

LEE T. C., COFFEY R. J., MACKIN J., COBB M., ROUTON J. CANARY J. J. (1973) The use of propranolol in the surgical treatment of thyrotoxic patients. *Ann. Surg.* **177**, 643–647.

LOWRY R. C., LOWE D., HADDEN D. R., MONTGOMERY D. A. D. and WEAVER J. A. (1971) Thyroid suppressibility: follow-up for two years after antithyroid treatment. *Br. Med. J.* **2**, 19–22.

MCDOUGALL I. R., GREIG W. R. and GILLESPIE F. C. (1971) Radioactive iodine ^{125}I therapy for thyrotoxicosis. *New Engl. J. Med.* **285**, 1099–1104.

MACKENZIE H. (1905) Graves' disease. *Br. Med. J.* **2**, 1077–1082.

MCLARTY D. G., ALEXANDER W. D., HARDEN R. MCG. and CLARK D. H. (1969) Results of treatment of thyrotoxicosis after postoperative relapse. *Br. Med. J.* **3**, 200–203.

MICHIE W. (1970) The recurrent laryngeal nerves at thyroidectomy. *Lancet* **1**, 1227–1228.

MICHIE W., HAMER-HODGES D. W., PEGG C. A. S., ORR F. G. G. and BEWSHER P. D. (1974) Beta-blockade and partial thyroidectomy for thyrotoxicosis. *Lancet* **1**, 1009–1011.

MICHIE W., PEGG C. A. S. and BEWSHER P. D. (1972) Prediction of hypothyroidism after partial thyroidectomy for thyrotoxicosis. *Br. Med. J.* **1**, 13–17.

MICHIE W., STOWERS J. M., DUNCAN T., PEGG C. A. S., HAMER-HODGES D. W., HEMS G., BEWSHER P. D. and HEDLEY A. J. (1971) Mechanism of hypocalcaemia after thyroidectomy for thyrotoxicosis. *Lancet* **1**, 508–514.

MOOSMAN D. A. and DE WEESE M. S. (1968) The external laryngeal nerve as related to thyroidectomy. *Surg. Gynecol. Obstet.* **127**, 1011–1016.

MUKHTAR E. D., SMITH B. R., PYLE G. A., HALL R. and VICE P. (1975) Relation of thyroid-stimulating immunoglobulins to thyroid function and effects of surgery, radioiodine, and antithyroid drugs. *Lancet* **1**, 713–715.

MURAKAMI Y. and KINCHNER J. A. (1971) Vocal cord abduction by regenerated recurrent laryngeal nerve: an experimental study in the dog. *Arch. Otolaryngol.* **94**, 64–68.

MURLEY R. S. and PETERS P. M. (1961) Inadvertent parathyroidectomy. *Proc. R. Soc. Med.* **54**, 487–489.

MURLEY R. S. and RIGG B. M. (1968) Postoperative thyroid function and complications in relation to a measured thyroid remnant. *Br. J. Surg.* **55**, 757–760.

NOFAL M. M., BEIERWALTES W. H. and PATNO M. E. (1966) Treatment of hyperthyroidism with sodium iodide. *JAMA* **197**, 605–610.

OLSEN W. R., NISHIYARIK R. H. and GRABER L. W. (1970) Thyroidectomy and hyperthyroidism. *Arch. Surg.* **101**, 175–180.

PEGG C. A. S., STEWART D. J., BEWSHER P. D. and MICHIE W. (1973) The surgical management of thyrotoxicosis. *Br. J. Surg.* **60**, 765–769.

PEMBERTON J. DE J. (1930) Recurring exophthalmic goitre: its relation to amount of tissue preserved in thyroid gland. *JAMA* **94**, 1483–1489.

VON RECKLINGHAUSEN F. (1891) *Festschrift Rudolf Virchow zu seinem* 71. Geburstage. Berlin, p. 20.

RIDDELL V. (1962) Thyrotoxicosis and the surgeon. *Br. J. Surg.* **49**, 465–496.

RIDDELL V. (1970) Thyroidectomy: prevention of bilateral recurrent nerve palsy. *Br. J. Surg.* **57**, 1–11.

ROWLANDS D. J., HOWITT G. and MARKHAM P. (1965) Propranolol (Inderal) in disturbances of cardiac rhythm. *Br. Med. J.* **2**, 891–894.

SAENGER E. L., THOMA G. E. and TOMPKINS E. A. (1968) Incidence of leukaemia following treatment of hyperthyroidism: preliminary report on the cooperative thyrotoxicosis follow-up study. *JAMA* **205**, 855–862.

SANDERSON P. H., MARSHALL F. and WILSON R. E. (1960) Calcium and phosphorus homeostasis in the parathyroidectomised dog: evaluation by means of ethylenediamine tetraacetate and calcium tolerance tests. *J. Clin. Invest.* **39**, 62–70.

SATTLER H. (1908) *Basedow's Disease*. English translation by MARCHAND G. W. and MARCHAND J. F. (1952). New York, Grune & Stratton, p. 284.

SCHLICKE C. P. (1974) Recent trends in thyroid surgery. *Am. J. Surg.* **128**, 269–275.

SIRIBODHI G., SUNMAKER W., ATKINS J. P. and BONNER F. J. (1963) Electromyographic studies of laryngeal nerve paralysis and regeneration of laryngeal motor nerves in dogs. *Laryngoscope* **73**, 148–164.

SMITH I. and MURLEY R. S. (1965) Damage to the cervica sympathetic system during operation on th thyroid gland. *Br. J. Surg.* **52**, 673–675.

STARR P., JOFFE H. L. and OETTINGER L. (1964) Lat results of I^{131} treatment of hyperthyroidism i seventy-three children and adolescents. *J. Nuc Med.* **5**, 81-89.

TAYLOR G. W. and PAINTER N. S. (1962) Size of th thyroid remnant in partial thyroidectomy fo toxic goitre. *Lancet* **1**, 287–289.

THEILEN E. O., WILSON W. R. and TUTUNGI F. J. (1963 The acute haemodynamic effects of alpha methyldopa in thyrotoxic patients and norma subjects. *Metabolism* **12**, 625–630.

THOMPSON W. O., MORRIS A. E. and THOMPSON P. K (1930) Thyrotoxicosis following subtotal thyroidectomy for exophthalmic goiter. *Arch. Intern Med.* **46**, 946–978.

THORNELL W. C. (1950) New intralaryngeal approac for arytaenoidectomy in treatment of bilatera abductor vocal cord paralysis. *J. Clin. Endocrinol* **10**, 1118–1125.

TURNER P., GRANVILLE-GROSSMAN K. L. and SMART J. V (1965) Effects of adrenergic receptor blockade o the tachycardia of thyrotoxicosis and anxiet state. *Lancet* **2**, 1316–1318.

VAN WELSUM M., FELTKAMP T. E. W., DE VRIES M. J. DOCTOR R., VAN ZIJL J. and HENNEMANN G. (1974 Hyperthyroidism after thyroidectomy for Graves disease: a search for an explanation. *Br. Med. J* **4**, 755–757.

VOLPÉ R., EDMONDS M., LAMKI L., CLARKE P. V. an ROW V. V. (1972) The pathogenesis of Graves disease. *Staff Meet. Mayo Clin.* **47**, 824–834.

WADE J. H. S. (1961) The recurrent laryngeal nerve *Proc. R. Soc. Med.* **54**, 875–876.

WALDSTEIN S. S., WEST G. H., LEE W. Y. and BRONSK D. J. (1964) Guanethidine in hyperthyroidism *JAMA* **189**, 609–612.

WELSH D. A. (1898) Concerning the parathyroi glands: a critical anatomical and experimenta study. *J. Anat. Physiol.* **32**, 292–307.

WERNER S. C., WEGELIUS O., FIERER J. A. and HSU K. C (1972) Immunoglobulins (E, M, G) and complement in the connective tissues of the thyroid glan in Graves' disease. *New Engl. J. Med.* **287**, 421-425.

WILLIAMSON R. T. (1896) Remarks on prognosis i exophthalmic goitre. *Br. Med. J.* **2**, 1373–1374.

WILSON W. R., THEILEN E. O. and FLETCHER F. W. (1964 Pharmacodynamic effects of beta-adrenergi receptor blockade in patients with hyper thyroidism. *J. Clin. Invest*, **43**, 1697–1703.

WOLFF J. and CHAIKOFF I. L. (1948) Plasma inorgani iodide as homeostatic regulator of thyroi function. *J. Biol. Chem.* **174**, 555–564.

Br. J. Surg. Vol. 62 (1975) 683–688

Surgical treatment of thyrotoxicosis: results of 272 operations with special reference to preoperative treatment with anti-thyroid drugs and L-thyroxine

PETER HEIMANN AND JAN MARTINSON*

SUMMARY

From 1959 to 1970, 272 operations for thyrotoxicosis were performed. Most of the patients received anti-thyroid drugs and thyroid hormones preoperatively. The patients were continuously followed up. The primary results with low morbidity and no mortality as well as the long term results with a low rate of recurrence and a relatively high incidence of thyroid substitution are discussed. A safe and effective programme for surgical treatment of thyrotoxicosis is described. Anti-thyroid drugs and thyroid hormones should be administered as the method of choice in preparing these patients for surgery.

THE results of surgical treatment of thyrotoxicosis have improved dramatically during the past 10–15 years. One reason is that there are now three different forms of treatment: anti-thyroid drugs, radio-iodine therapy and surgery. Each treatment can be used for a different group of patients and therefore a better selection of patients for surgical treatment can be made. Another reason is that patients undergoing surgery after preoperative treatment with anti-thyroid drugs *and* L-thyroxine are easier to operate on, with a small operative morbidity and without risk of a post-operative thyrotoxic crisis. The patient is euthyroid, the thyroid is empty of thyroxine (due to inhibition of synthesis by anti-thyroid drugs) and the gland is unstimulated (due to the TSH-inhibiting effect of thyroxine therapy). The combination of anti-thyroid drugs and thyroxine was first introduced by Fraser and Wilkinson in 1953. Bergfelt et al. used this treatment preoperatively in 1961. The effect of such treatment on the thyroid has been studied by various methods, e.g. histological studies (Eggen and Seljelid, 1973) and electron microscopy studies (Heimann 1966, 1967), which have shown that the histological picture of the adequately pretreated gland is very similar to that of the normal gland or the non-toxic goitre. In this paper we report our clinical experience and the results of surgical treatment of thyrotoxicosis.

Patients

All the patients with thyrotoxicosis presenting to the Department of Surgery II, Sahlgrenska Hospital, Göteborg, during the period from 1 January 1959 to 31 December 1970 are included. The series consists of 395 patients with thyrotoxicosis; 271 were treated surgically and 124 were treated medically or with radio-iodine, according to the principles of selection shown in *Fig.* 1. Of the 271 surgically treated patients, 48 were male and 223 female (ratio 1 : 5). The age distribution and different histological diagnoses are shown in *Fig.* 2. Of the operations, 258 were primary and 14 were reoperations (one of our patients was operated on twice).

Methods

Preoperative diagnostic programme

Thyroid function was assessed from the serum protein-bound iodine and the T_3 test. In difficult cases the ^{131}I uptake curve and/or the T_3 inhibition test were used.

In cases with goitre X-rays of the neck and thorax were carried out. Scintigraphy was always performed in cases with nodular goitre and in those with adenoma.

For assessment of the parathyroid function estimations of serum calcium, phosphorus, albumin and creatinine were made.

The recurrent laryngeal nerve was studied by laryngoscopy. Electrocardiogram, chest X-ray, haemoglobin and blood sedimentation rate were performed routinely.

The most important parts of the preoperative investigation are obtaining a complete history of the disease and evaluation of the clinical status. In cases with exophthalmos an ophthalmologist should be involved. All these investigations can be performed on an outpatient basis. Only patients with severe thyrotoxicosis or other complicating disease need hospitalization.

Preoperative treatment

This was performed according to the following principles:

1. The patient was started on an anti-thyroid drug, carbimazole (or methimazole) 10 mg q.i.d. or propylthiouracil 100 mg q.i.d.

2. If the thyrotoxic symptoms were severe and/or the goitre large it was often necessary to give a larger dosage. In most cases 10 mg six times a day (100 mg six times a day for propylthiouracil) were sufficient. If still larger doses were needed the patient was treated in hospital. All patients can be made euthyroid with this treatment if adequate dosage is given over a sufficient period of time.

---

* Department of Surgery II, Sahlgrenska Hospital, University of Göteborg, Sweden.

Present address of P. Heimann: Department of Surgery, University of Bergen, Haukeland sykehus, Bergen, Norway.

Present address of J. Martinson: Department of Surgery, Centrallasarettet, Lidköping, Sweden.

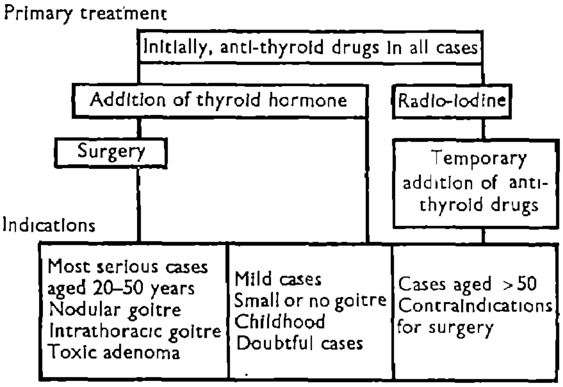

Primary treatment
Initially, anti-thyroid drugs in all cases
Addition of thyroid hormone
Radio-iodine
Surgery
Temporary addition of anti-thyroid drugs
Indications
Most serious cases aged 20–50 years
Nodular goitre
Intrathoracic goitre
Toxic adenoma
Mild cases
Small or no goitre
Childhood
Doubtful cases
Cases aged >50
Contraindications for surgery

Fig. 1. Selection of patients with thyrotoxicosis for surgery.

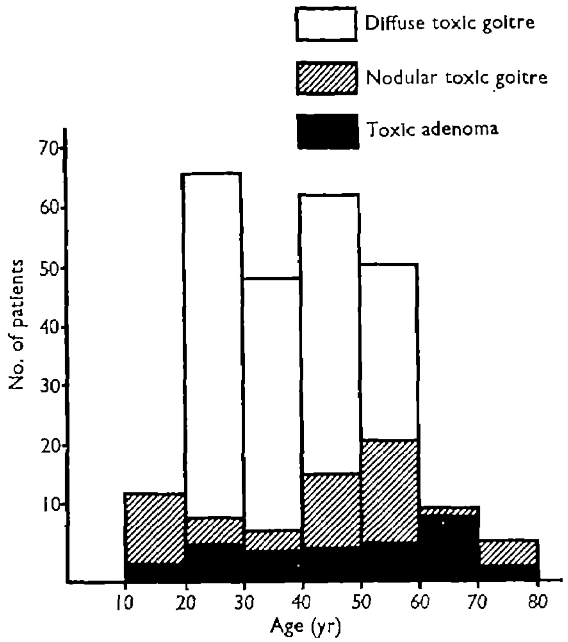


Fig. 2. Age distribution related to the diagnosis.

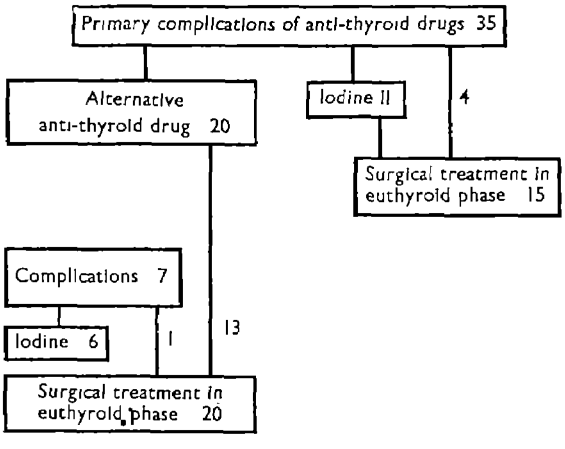

Primary complications of anti-thyroid drugs 35
Alternative anti-thyroid drug 20
Iodine 11
4
Surgical treatment in euthyroid phase 15
Complications 7
Iodine 6
1
13
Surgical treatment in euthyroid phase 20

Fig. 3. Alternative treatment of 35 patients who developed side effects with the initial anti-thyroid drug.

We did not perform repeated white blood cell counts. All the patients received written information about the side effects of the preparation used and were told to contact their doctor or the hospital as soon as they noticed any symptoms.

3. When the patient became euthyroid—in most cases after 6–8 weeks—the dosage of the anti-thyroid drug was reduced to 5 mg q.i.d. for carbimazole (or methimazole) or 50 mg q.i.d. for propylthiouracil. The patient was told that it was necessary to continue with this dosage until the day of operation.

4. In addition to this reduced dosage of anti-thyroid drug the patient also received thyroxine (L-thyroxine) 0·20 mg every morning. (It is also possible to give tri-iodothyronine 0·02 mg t.d.s. or q.i.d.) Older patients with nodular goitre or very small (< 50 kg) patients received 0·15 mg thyroxine once daily. This combined treatment was continued for at least 4 weeks, and it was often advisable to continue it for longer. Most of our patients were treated for a varying period of time (from 1 to 6 months). Thus it was possible to operate on the patient at a time suitable for the patient, surgeon and hospital.

Carbimazole was the most frequently used anti-thyroid drug (148 patients), methimazole was used in 73 cases and propylthiouracil in 27. If preoperative treatment had been started elsewhere, we always continued with the drug used initially.

Not all the patients were pretreated with anti-thyroid drugs and thyroxine, because of our electron microscopy study, in which different methods of treatment were compared (Heimann, 1966). Most of the toxic adenomas were operated on without preoperative treatment. Some patients with complications caused by the preoperative treatment were transferred to another group (*Fig.* 3).

Operative technique

All the patients were operated on under general endotracheal anaesthesia. The surgical procedure has previously been described (Heimann, 1962) and therefore is only briefly reviewed here. A Kocher collar incision was used. The infrahyoid muscles were separated and the dissection was continued cautiously, not permitting any bleeding. The inferior thyroid arteries were ligated but not divided. The superior thyroid arteries were ligated twice, but likewise not divided. As a rule the recurrent laryngeal nerve and the parathyroid glands were identified but not freed. In general when a subtotal resection was performed a small remnant of thyroid tissue was left. Thereafter the capsule was sutured with 2/0 chromic catgut. The best possible haemostasis was obtained. The muscles were repaired with chromic catgut and the platysma with interrupted subcutaneous 4/0 plain catgut. The skin was apposed with clips. All ligatures were of chromic catgut except those on the inferior and superior thyroid arteries, which were of black silk. In all cases the excised specimens were sent for pathological examination.

The types of operation performed are related to the diagnosis in *Table I*.

Postoperative management

Drainage of the wound was continued for 24 hours. Removal of every second clip was carried out after 48 hours and the rest after 96 hours. The patient was discharged from hospital on the fourth or fifth postoperative day.

Daily measurements of serum calcium, pulse and temperature were performed. The patient was permitted to drink from the first postoperative day. No postoperative parenteral feeding or fluids were given. The patient was mobilized on the first postoperative day.

Before leaving the hospital the patient was referred for postoperative laryngoscopy. Patients at risk of thyroid deficiency received thyroxine substitution immediately after operation. Patients with toxic adenoma were sent for postoperative thyroid scanning after 3–4 weeks.

Repeat studies of the patient were performed at 1 month (at the time of return to work), 4 months (estimation of protein-bound iodine etc. for euthyroidism), 1 year and thereafter once every year. Patients with complications or other complicating diseases were studied more often. All the patients were continuously followed up in the outpatients' department.

Results

Preoperative complications

Side effects of the anti-thyroid treatment were observed in 42 cases (*Table II*). The incidence of side effects was significantly higher in patients treated with propylthiouracil or methimazole (21–22 per cent) than in the group treated with carbimazole (13 per cent). Most of the side effects were slight and disappeared after reducing the dosage, changing the drug or on complete withdrawal of treatment. No serious side effects (agranulocytosis and/or icterus) were observed in patients treated with carbimazole (*Table III*). The influence of side effects on further preoperative treatment is shown in *Fig*. 3. All the patients could be operated on in a non-toxic phase. In 11 cases the side effects were negligible and did not influence further treatment. In 11 other cases preoperative treatment was continued with iodine. Twenty patients were changed to another anti-thyroid drug. This change was successful in 13 cases while 7 patients showed new or the same complications with the alternative drug. Six of these received iodine and the remaining one was operated on without further preoperative treatment as she was considered to be euthyroid.

Table I: TYPE OF OPERATION PERFORMED RELATED TO DIAGNOSIS

Diagnosis	No. of cases	%	Operation Bilateral	Unilateral
Diffuse toxic goitre	198	73	199	0
Nodular toxic goitre	49	18	32	17
Toxic adenoma	24	9	2	22
Total	271	100	233	39

Table II: SIDE EFFECTS OF PREOPERATIVE DRUG THERAPY

Drug	No. of treatments	Side effects No.	%
Carbimazole	148	20	13
Methimazole	73	16	22
Propylthiouracil	27	6	21

Table III: TYPES OF SIDE EFFECTS OBSERVED

Side effect	Incidence of side effects (%) Carbimazole	Methimazole	Propylthiouracil
Leucopenia	2	0	7
Agranulocytosis	0	2·7	0
Icterus	0	1·3	0
Allergic skin symptoms	7	10	7
Non-specific symptoms	4	8	7

Table IV: INCIDENCE OF PERSISTENT RECURRENT LARYNGEAL PARALYSIS

Type of operation	No. of cases	Paresis No.	%
All operations	272	1	0·4
Reoperation	14	1	7·0
Primary operation	258	0	—

Table V: INCIDENCE OF POSTOPERATIVE HYPOPARATHYROIDISM

Type of operation	No. of cases	Hypocalcaemia No.	%
All operations	272	6	2·2
Reoperation	14	3	21·0
Total thyroidectomy	2	1	
Surgeon not belonging to our thyroid team	20	1	5·0
Primary operation by our thyroid team	236	1	0·4

Table VI: HOSPITALIZATION TIME RELATED TO PREOPERATIVE TREATMENT

Preoperative treatment	Hospitalization time (d)
Anti-thyroid drug + thyroxine	6·5
Anti-thyroid drug + iodine	18
Iodine	32
No preoperative treatment	7

Postoperative complications

There were no operative deaths. There was no case of postoperative thyrotoxic crisis in the patients treated preoperatively with anti-thyroid drugs. One patient developed a postoperative thyrotoxic crisis after incomplete preoperative treatment with iodine.

Recurrent laryngeal nerve paralysis: Our follow-up showed that only 1 patient had a persistent paralysis (*Table IV*). This patient was one of the 14 patients undergoing reoperation. Temporary bilateral paresis was observed in 6 women; 5 of these patients were less than 30 years (7 per cent) and one was over 30 (0·8 per cent). These bilateral transient paralyses disappeared spontaneously, mostly within a week.

Postoperative hypocalcaemia: The total number of patients with permanent hypocalcaemia needing treatment was 6 (2·2 per cent; *Table V*). The incidence in the series of cases with subtotal operation performed by trained thyroid surgeons was 0·4 per cent.

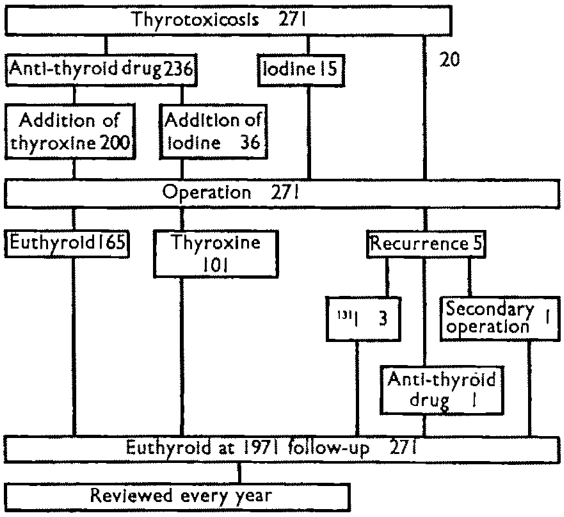


Fig. 4. Summary of the treatment of 271 cases of thyrotoxicosis undergoing surgery.

Hospitalization time

Patients treated preoperatively with an anti-thyroid drug and thyroxine had a similar short hospital stay to the small group of patients with toxic adenoma who received no preoperative treatment. As all treatment with iodine is given to inpatients, the period in hospital for these smaller groups exceeded that of the thyroxine-treated group significantly (*Table VI*).

Late results

Follow-up of the patients for this report was completed in 1971. The observation time was therefore 1–13 years.

Recurrent thyrotoxicosis occurred in 5 cases (2 per cent); 1 underwent reoperation, 3 received radio-iodine and 1 was successfully treated with an anti-thyroid drug. At follow-up in 1971 all 271 patients operated on were euthyroid.

Postoperative hypothyroidism and substitution therapy

The following patients received postoperative substitution from the time of operation: (*a*) cases with strong lymphocytic infiltration; (*b*) cases with a high titre of thyroid antibodies; (*c*) cases with endocrine exophthalmos; (*d*) cases in which an unusually large resection was performed; (*e*) cases undergoing total thyroidectomy; (*f*) cases of malignancy (3 patients). Accordingly 81 patients were given thyroxine substitution (30 per cent).

Among the remaining 190 cases, hypothyroidism was diagnosed and treated in 20 cases (10·5 per cent). A need for postoperative thyroid substitution treatment therefore was found in 38 per cent of the whole series. The incidence was highest in patients with nodular toxic goitre (50 per cent) and lowest in cases with toxic adenoma (8 per cent). The postoperative dosage of L-thyroxine was generally 0·20 mg once a day. No patient received more than 0·20 mg and some were on a lower dosage (0·10 or 0·15 mg).

Other findings

Among the 271 patients operated on for thyrotoxicosis, there were 3 parathyroid adenomas and 9 thyroid tumours of which 4 were malignant. The incidence of parathyroid tumours was 1 per cent and the incidence of thyroid tumours 3 per cent.

Discussion

Many reports of the results of surgical treatment of thyrotoxicosis have been published (Heimann, 1969; Caswell, 1972; Barnes and Gann, 1974; Gillquist, 1974). In this report we want to stress the following important principles:

1. The selection of patients for surgical treatment (*Fig*. 1).
2. Preoperative treatment with anti-thyroid drugs and thyroxine (used in 74 per cent of our series) (*Fig*. 4).
3. The subsequent use of subtotal bilateral resection with ligation of the inferior thyroid artery.
4. The liberal postoperative use of thyroxine in substitution therapy (*Fig*. 4).
5. The treatment of recurrence with methods other than surgery, only 1 patient in our series being operated on twice.

There was no mortality and the surgical morbidity was low. The long term results so far are promising as regards recurrence of the disease (2 per cent). Postoperative treatment with thyroxine is easy to manage and only one investigation per year is necessary. All the patients are reminded to attend for these studies in order to be sure of an adequate follow-up, which is an important part of the treatment.

Treatment with anti-thyroid drugs reduces or abolishes the synthesis of thyroxine and tri-iodothyronine, the level of protein-bound iodine falls and the patient becomes euthyroid. If the treatment continues at a sufficient dosage for full blockage of hormone synthesis the patient becomes hypothyroid and the thyroid gland will be stimulated by an increasing amount of circulating TSH. It is important both for the clinical course of the disease (especially as regards the development of goitre and/or exophthalmos) and for the surgical approach that the patient remains euthyroid and that TSH secretion is continuously inhibited. We therefore give the patients thyroxine (or tri-iodothyronine) as soon as they become euthyroid. At operation the patient is euthyroid and the thyroid gland is empty of thyroxine and tri-iodothyronine. There is no postoperative toxic reaction (rise of pulse or temperature, or nervous symptoms).

The preoperative treatment is sometimes complicated by undesirable side effects of the anti-thyroid drug. Change to another drug or to iodine or in some cases reducing the dosage used nearly always makes it possible to continue treatment and to prepare the patient and the thyroid gland adequately for surgery. In our series carbimazole seemed to be the drug of choice.

Postoperative complications were rare. Thyroid surgery in experienced hands should not carry any postoperative mortality. In this regard the present series is comparable with other larger series (Heimann, 1962). The patients in the latter series (966 cases of thyrotoxicosis treated surgically) were all treated preoperatively with iodine. An important difference between the series treated with iodine and that treated with anti-thyroid drugs and thyroxine is that a postoperative thyrotoxic crisis cannot occur after adequate preoperative treatment with anti-thyroid drugs. There is no excess of thyroid hormones in the completely inhibited gland.

Persistent paralysis of the recurrent laryngeal nerve is a serious complication. It is well known that this complication is frequently seen after difficult reoperations and in radical neck surgery. If thyrotoxic patients are operated on without a constant good view of the operation area the nerve can easily be damaged. Bleeding has to be avoided and the exposure must at all times be adequate. We operate slowly with full control of all bleeding. All vessels, even the smallest, are ligated. In our series of primary subtotal bilateral resections for thyrotoxicosis (258 cases) we had no case of persistent paralysis of the recurrent nerve. An interesting observation in our series concerned 6 female patients with temporary postoperative bilateral paresis of the nerve. In all cases this paresis did not occur immediately after surgery. At extubation there was no bilateral paresis. Symptoms suddenly occurred during the first 24 hours postoperatively. We used to treat such patients by tracheostomy until the paresis disappeared after 5–8 days. Our last cases were treated without tracheostomy. The patients were sedated and the inspired air moistened. They were told that there would soon be a spontaneous regression and complete recovery. The observation of these patients was intensive. It is difficult to explain this temporary paresis. Most of the patients were anxious young women. It is possible that it is a toxic effect (lidocaine adrenaline used for subcutaneous infiltration?, anaesthetic drug?, preoperative treatment?); one also has to ask if it is a real paresis or perhaps a traumatic damage of the vocal cords? Intubation and the maximal dorsiflexion of the neck during surgery could be responsible. Respiratory difficulties begin during the first hours after extubation and disappear completely as suddenly. It therefore seems to be a local affection probably caused by several factors.

Postoperative hypocalcaemia is the most severe complication, for it is necessary to give these patients lifelong treatment with approximately four blood studies a year. The risk is greatest in connection with reoperation. In our series hypoparathyroidism was observed in 3 of 14 (21 per cent) reoperations. Reoperation should therefore be avoided, which means adequate and complete primary operations and nonsurgical treatment of recurrences.

Of the 6 cases with hypocalcaemia, 3 occurred after primary surgery, one in connection with one of our two total thyroidectomies for thyrotoxicosis and one among the small group of 20 patients who were not operated on by members of our thyroid team. In 236 primary subtotal thyroidectomies for thyrotoxicosis performed by trained thyroid surgeons only 1 patient developed postoperative hypoparathyroidism; an incidence of 0·4 per cent.

Thus, primary subtotal thyroidectomy for thyrotoxicosis after preoperative treatment with antithyroid drugs and thyroxine and performed by experienced surgeons has no mortality and a very low postoperative morbidity. Surgery therefore offers an effective treatment of thyrotoxicosis. The long term results are good. Our aim is to avoid recurrence of thyrotoxicosis, for it represents such a difficult therapeutic problem. In order to detect hypothyroidism and recurrent goitre all our patients are under continuous observation and review after operation. Cases in which the risk of hypothyroidism is greater receive prophylactic treatment with thyroid hormone. With our programme of therapy of thyrotoxicosis we can offer the patient treatment which in all cases leads to euthyroidism. Most patients are cured by preoperative treatment and surgery, approximately every third patient also needs postoperative substitution and a very few need additional treatment with radio-iodine or antithyroid drugs; all have to be followed up (*Fig.* 4).

An important point in this programme is the fact that the treatment brings the patient to a steady euthyroid state more quickly than radio-iodine treatment or medical treatment. Preoperative treatment can be given on an outpatient basis in most cases. The majority of patients can also work from the time when they become euthyroid until the day before operation. Hospitalization time is minimal (6–7 days), and postoperatively most patients are back at work after 4 weeks.

An observation worth mentioning is the detection at operation of thyroid and parathyroid tumours. Thyroid carcinoma can be associated with thyrotoxicosis and is often undetected by diagnostic measures such as scanning or aspiration needle biopsy. We found such tumours in 4 per cent of our series as a consequence of our surgical technique with full dissection of arteries, nerve, parathyroids, especially the dorsal aspect of the thyroid gland and the paratracheal thyrothymic fascia.

Conclusions

Preoperative preparation with anti-thyroid drugs in combination with thyroxine or tri-iodothyronine allows safe surgical treatment of thyrotoxicosis. This corresponds with structural and ultrastructural results and pathophysiological findings. We would recommend the following programme:

1. Surgical treatment should be chosen for young patients (20–50 years) with diffuse toxic goitre or toxic adenoma and for older patients in whom nodular goitre is producing mechanical symptoms.

2. Preoperative treatment should be instituted and continued with an anti-thyroid drug until the patient is completely euthyroid, followed by a maintenance dosage of the drug sufficient to block all thyroid hormone synthesis. In addition, the patient should receive substitution thyroxine (0·20 mg daily) or tri-iodothyronine (0·020 mg four times daily). Thyroid

hormone should be given for at least 4 weeks preoperatively, most of our patients receiving this treatment for 2–4 months.

3. Surgery should be performed by surgeons with special experience of this work. Bleeding has to be avoided. All important structures such as vessels, nerves and the parathyroids must be identified. Both the superior and inferior thyroid arteries should be ligated. The aim of the resection should be to avoid recurrence of the thyrotoxic symptoms.

4. The care of the patients should include pre- and postoperative laryngoscopy and daily serum calcium estimation. Patients who are considered to carry a larger risk of hypothyroidism should receive prophylactic thyroxine treatment postoperatively. All patients should be followed up, probably for the rest of their lives.

5. Recurrence of thyrotoxicosis should be treated by methods other than surgery.

With this programme we can offer the patient a safe, quick and effective way to euthyroidism. Preoperative treatment with anti-thyroid drugs and thyroid hormones has real advantages and should be adopted as the method of choice.

References

BARNES H. V. and GANN D. S. (1974) Choosing thyroidectomy in hyperthyroidism. *Surg. Clin. North Am.* **54**, 289–307.

BERGFELT G., LJUNGGREN J.-G. and HEDBERG K. (1961) Preoperative treatment of thyrotoxicosis with antithyroid drugs and thyroxine. *J. Clin. Endocrinol.* **21**, 72–79.

CASWELL T. H. (1972) Result of surgical treatment for hyperthyroidism. *Surg. Gynecol. Obstet.* **134**, 218–220.

EGGEN P. C. and SELJELID R. (1973) The histological appearance of hyperfunctioning thyroids following various preoperative treatments. *Acta Pathol. Microbiol. Scand.* **81**, 16–20.

FRASER R. and WILKINSON M. (1953) Simplified method of drug treatment for thyrotoxicosis. *Br. Med. J.* **1**, 481–484.

GILLQUIST J. (1974) Preoperative treatment of hyperthyroidism. Effect on primary postoperative complications. *Acta Chir. Scand.* **140**, 23–26.

HEIMANN P. (1962) Atoxic and toxic goitre. *Acta Chir. Scand.* (*Suppl.*) 289.

HEIMANN P. (1966) Ultrastructure of human thyroid. A study of normal thyroid, untreated and treated diffuse, toxic goitre. *Acta Endocrinol.* (*Suppl.*) (*Kbh.*) **53** 110.

HEIMANN P. (1967) Ultrastructure of human thyroid in thyrotoxicosis. In: IRVINE W. J. *Thyrotoxicosis.* Edinburgh, Livingstone, pp. 155–163.

HEIMANN P. (1969) Pathophysiological aspects of surgical treatment of thyroid disease. *Prog. Surg.* **7**, 1–55.

Br. J. Surg. Vol. 62 (1975) 689–691

Carcinoma arising in thyroglossal duct remnant: case reports and review of the literature

PRAKASH C. SAHARIA*

SUMMARY

Two cases of thyroglossal duct cyst carcinoma are presented and the world literature is reviewed. There are only 74 cases reported to date. In nearly all the cases the clinical diagnosis was thyroglossal cyst. Although the great majority of the tumours were papillary adenocarcinomas, 13·15 per cent were of other histological types. The treatment has been quite variable, but the most common initial treatment was Sistrunk's (1928) operation. Following the establishment of the diagnosis of malignancy, thyroidectomy was done in several cases, but it failed to show any evidence of malignancy in most of the thyroids removed, which establishes firmly the de novo origin of these tumours from the thyroglossal duct remnant. In only one case had tumour disseminated to distant organs, the lung, liver, etc. The scepticism as to whether some of the carcinomas associated with thyroglossal duct remnants may not in fact represent metastases from a small primary tumour of thyroid gland is examined. It appears that, though a possibility of primary or metastatic tumour in the thyroid does exist, the probability does not appear to be high. From our own experience it is suggested that local excision followed by radiotherapy, irrespective of recurrence, may be worth considering for the treatment of such carcinomas.

CARCINOMA arising in a thyroglossal duct remnant is rare. Only 74 cases have been reported in the world literature to date. Most have been papillary adenocarcinomas, but squamous cell lesions have also been documented. The present report adds 2 cases to the literature and documents common clinical data for this group of unusual tumours.

Case reports

Case 1: An 81-year-old white female was admitted to Derby City Hospital (Eng.) in February 1971 with a mass in her neck of 4½ months' duration. It was painless but increasing in size rapidly. There were no related symptoms. Physical examination revealed a 4 × 5-cm mass at the level of the thyroid cartilage, slightly to the left of the midline. It was smooth, spherical in shape and firm in consistency. It was adherent to the hyoid bone, but was not attached to the overlying skin. The mass moved with swallowing and protrusion of the tongue. There were no palpable cervical lymph nodes, and the thyroid gland felt normal in size and consistency. X-ray of the chest showed no abnormality.

Excision of the mass, including the left hyoid bone, strap muscles and part of the thyroid cartilage and thyroglossal duct up to the foramen caecum, was carried out *en bloc* through a collar incision. The thyroid gland was exposed and was found to be normal. Exploration of the neck for enlarged cervical glands was negative.

Examination of the specimen revealed a cyst, 6 cm in diameter, containing a nodule in the wall. The wall of the cyst was lined by squamous cell epithelium and the nodule itself was a well-differentiated squamous cell carcinoma invading the surrounding tissue and strap muscles.

The postoperative course was uneventful and the patient has remained free of any evidence of recurrence for 3 years following surgery.

Case 2: A 54-year-old white male was admitted to Wordsley Hospital, Worcester, in August 1970 with a neck mass of 3 months' duration.

Physical examination revealed a smooth, cystic, spherical, non-tender, 5 × 4-cm mass overlying the left thyroid cartilage. The mass moved with swallowing and protrusion of the tongue. The thyroid gland felt normal in size and consistency. There were no enlarged cervical lymph nodes.

The mass was removed through a collar incision along with the adherent strap muscles, left hyoid bone, part of the thyroid cartilage and the thyroglossal duct *en bloc*. The thyroid gland was exposed and was found to be normal. No enlarged cervical glands were detected.

Examination of the specimen revealed a cyst 5 × 4 × 2 cm with a thick fibrous wall and an irregular fibrotic plaque in the wall of the cyst. Microscopically, the wall was fibrotic with foci of active and chronic inflammation. In parts of the cyst, groups of papillary elements were found which consisted of orderly, well-differentiated neoplastic cells consistent with papillary adenocarcinoma. Some follicular neoplastic elements containing colloid were also present. Tumour cells were observed in the overlying strap muscles (*Fig.* 1).

The patient's postoperative recovery was uneventful. In view of the muscle invasion, the possibility of incomplete excision and the fact that the patient was a poor surgical risk, a course of radiotherapy was given.

There is no evidence of recurrence after 3½ years' follow-up.

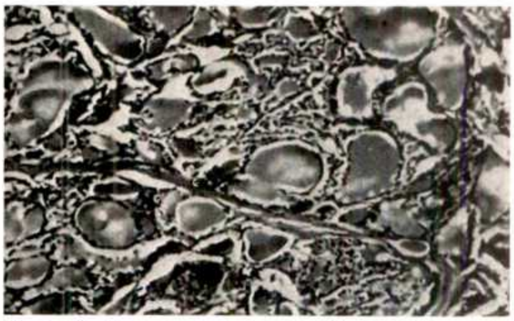


Fig. 1. Papillary adenocarcinoma with follicular neoplastic elements containing colloid. (× 180.)

Discussion

The thyroid gland forms at about the fourth week of embryonic life from a median diverticulum of the ventral pharyngeal wall at a position marked in adult life by the foramen caecum. As the thyroid gland migrates downwards, it forms a duct behind it in its path. The duct can be lined by squamous, columnar or transitional epithelium. Ordinarily the duct disappears at the sixth or seventh week of fetal life.

---

* Department of Surgery, The Johns Hopkins University, Baltimore, Maryland, USA.

Table I: LOCATION OF THE PRESENTING MASS IN THE NECK IN 76 CASES

Location of mass	No. of cases
Horizontal plane	
Midline	27
Left of midline	9
Right of midline	4
Not mentioned	36
Vertical plane	
Suprahyoid	14
Level of hyoid	9
Infrahyoid	16
Not mentioned	37

Table II: HISTOLOGY OF THE TUMOURS

Histology	No.	%
Papillary adenocarcinoma	66	86·84
Adenocarcinoma	2	2·6
Squamous cell carcinoma	5	6·57
Mixed follicular and papillary carcinoma	3	3·94

Table III: FOLLOW-UP OF 76 CASES

Time:	No. of cases:
Less than 5 years	47
5–10 years	13
11–15 years	5
16–20 years	2
Over 20 years	2
No follow-up	7

Incomplete obliteration, however, may lead to the development of a thyroglossal duct cyst which can appear in the midline anywhere between the foramen caecum and the suprasternal notch. In addition, thyroid rests can appear along this tract.

A survey of literature reveals 74 cases, and with the addition of the present 2 cases a total of 76 cases becomes available for analysis.

Clinically, the presenting symptom has generally been a gradually increasing cervical mass with variable location (*Table I*), in some cases associated with hoarseness and dysphagia. The known duration of the mass prior to surgery ranges from 10 days to 15 years. In the majority of cases the thyroid gland was reported to be normal on clinical and gross examination. Only 2 out of the 76 cases were associated with carcinoma of the isthmus and the right lobe of the thyroid (Rees and Brown, 1953; Mobini et al., 1974).

The pathological diagnoses were papillary adenocarcinoma in 66 cases, adenocarcinoma in 2, squamous cell carcinoma in 5 and mixed follicular and papillary carcinoma in 3 (*Table II*). The case reported by Dalgaard and Wetteland (1956) appears to have been a solid undifferentiated carcinoma and bears resemblance to the recently recognized medullary carcinoma with amyloid stroma.

Judd (1963) has stated that thyroid tissue in and around the thyroglossal duct is rarely encountered and that the occasional recording of papillary carcinoma of a thyroglossal cyst or sinus is erroneous. He contends that when a papillary carcinoma is encountered in this region the thyroid gland is always the source, and that if these were true carcinomas of thyroglossal duct or sinus origin they would be expected to be of the squamous cell type. Thyroid tissue has been found with thyroglossal duct remnants by others, however, in incidences ranging from 3 to 36·5 per cent (Ward et al., 1949; Choy et al., 1964). In addition, 4 cases of squamous cell carcinoma (Owen and Inglesby, 1927; Nachlas, 1950; Shepard and Rosenfeld, 1968; Mobini et al., 1974) arising from the thyroglossal duct have been reported. Furthermore, it is certainly possible that the stomodeal epithelium of the thyroglossal duct with its embryological potential of thyroidogenesis could produce a neoplasm resembling that of thyroid origin.

There is no unanimity of opinion regarding the surgical approach to such tumours. In most cases Sistrunk's (1928) operation was carried out. Following histological diagnosis of malignancy, further treatment has included re-excision of local tissues, bilateral block neck dissection, thyroid administration and radioiodine therapy (Zamrazil et al., 1971). Although thyroglossal duct cyst presents as a swelling slightly lateral to the midline, developmentally the thyroglossal duct cyst is a midline structure. Malignancy arising within it, therefore, can metastasize to lymph nodes on either side of the neck. Unilateral dissection has no place in the prophylaxis of spread, since it is impossible to predict which side (if either) will be the site of further metastasis. The follow-up of the reported cases ranges from 3 months to 28 years. Only 13 cases of recurrence have been reported. Twenty-nine cases have been followed up for more than 5 years (*Table III*). In only 1 case (Maxwell and Marchetta, 1960) were there distant metastases. The remaining instances were local recurrences treated by repeated local excisions or block dissection.

Because of the paucity of cases the long term prognosis is not clearly known. However, there is no reason to believe that this tumour should have different biological behaviour from carcinoma of the thyroid gland.

Acknowledgements

I would like to thank Mr A. W. Anderson, Consultant, City Hospital, Derby, and Mr M. Hershman, Consultant, Wordsley Hospital, near Stourbridge, for permitting me to publish their cases. I am also grateful to Dr John L. Cameron, Associate Professor of Surgery at the Johns Hopkins Hospital, Baltimore, for his help and guidance in preparing this manuscript.

References*

AKBARI Y., RICHTER R. M. and PAPADAKIS L. K. (1967) Thyroid carcinoma arising in thyroglossal duct remnants. *Arch. Surg.* **94**, 235–239.

ARONOFF B. L. (1952) Papillary thyroid cancer originating in thyroglossal cyst. *Am. Surg.* **18**, 362–371.

BERGERA J. J. and HORWITZ A. (1961) Papillary adenocarcinoma arising in a thyroglossal duct cyst. *Am. Surg.* **27**, 759–761.

---

* Including the references of all the cases reported to date.

BHAGAWAN B. S., GORWIDA RAO D. R. and WEINBERG T. (1970) Carcinoma of thyroglossal duct cyst: case report and review of literature. *Surgery* **67**, 281–292.

BOCHETTO J. F., MOUTOYE A. and SUNDE E. A. (1962) Papillary carcinoma of the thyroid in thyroglossal duct cysts. *Am. J. Surg.* **104**, 773–776.

BUTLER E. C., DICKEY J. R., SHILL O. S. and SHALAK E. (1969) Carcinoma of the thyroglossal duct remnant. *Laryngoscope* **79**, 264–271.

BYRNE J. J. (1952) Carcinoma in a thyroglossal cyst: report of a case. *Bost. Med. Q.* **3**, 86–89.

CHOY F. J., WARD R. and RICHARDSON R. (1964) Carcinoma of the thyroglossal duct. *Am. J. Surg.* **108** 361–369.

CLAWSON J. and KIMBALL H. (1962) Papillary adenocarcinoma of the thyroglossal duct cyst. *Ariz. Med.* **19**, 80–81.

CLUTE H. M. and CATTELL R. B. (1930) Thyroglossal cysts and sinuses. *Ann. Surg.* 92, 57–66.

COON W. W. (1965) Thyroid carcinoma—three unusual problems in diagnosis and management. *Am. J. Surg.* **109**, 629–633.

DALGAARD J. B. and WETTELAND P. (1956) Thyroglossal anomalies. *Acta Chir. Scand.* **111**, 444–455.

FALKINBURG L. W., HOEY W. O. and STUART J. R. (1966) Papillary adenocarcinoma arising in a thyroglossal duct cyst. *Oral Surg.* **21**, 358–360.

FISH J. and MOORE R. M. (1963) Ectopic thyroid tissue and ectopic thyroid carcinoma: a review of the literature and report of a case. *Ann. Surg.* **157**, 212–222.

GHENT W. R. and WAUGH D. (1960) Carcinoma in a thyroglossal remnant. *Can. J. Surg.* **4**, 79–81.

GURAIEB S. R. and VIETA L. J. (1962) Carcinoma in a thyroglossal cyst. Report of a case. *Arch. Otolaryngol.* **75**, 457–459.

HAYS L. L. and MARLOWE J. F. (1968) Papillary adenocarcinoma arising in thyroglossal duct cyst case report and literature review. *Laryngoscope* **78**, 2189–2203.

HILL D. P. (1961) Papillary carcinoma arising in a thyroglossal tract. *Can. Med. Assoc. J.* **85**, 791–793.

JAQUES D. A., CHAMBERS R. G. and OERTEL J. E. (1970) Thyroglossal tract carcinoma. *Am. J. Surg.* **120**, 439–446.

JUDD E. S. (1963) Thyroglossal duct cysts and sinuses. *Surg. Clin. North Am.* **43**, 1023–1032.

KALDERON A. E. and COHN J. D. (1966) Papillary adenocarcinoma in a thyroglossal cyst. Case report and review of literature. *Cancer* **19**, 839–843.

KEELING J. H. and OCHSNER A. (1959) Carcinoma in thyroglossal duct remnants. *Cancer* **12**, 596–600.

LATIMER R. G., SNOW E. and HICKS H. G. (1968) Papillary adenocarcinoma arising in a thyroglossal duct remnant. *Arch. Surg.* **97**, 161–162.

MARSHALL S. F. and BECKER W. F. (1949) Thyroglossal cysts and sinuses. *Ann. Surg.* **129**, 642–651.

MAXWELL W. T. and MARCHETTA F. E. (1960) Papillary adenocarcinoma of the thyroglossal duct tract. *Arch. Surg.* **80**, 224–225.

MOBINI J., KROUSE T. B. and KLINGHOFFER J. F. (1974) Squamous cell carcinoma arising in a thyroglossal duct cyst. *Am. Surg.* **40**, 290–294.

MOULIK B. N., PRAKASH A., KUMAR V. and SAMPATH A. (1974) Carcinoma of thyroglossal duct remnant: case report and review of the literature. *Am. Surg.* **40**, 248–252.

NACHLAS N. E. (1950) Thyroglossal duct cysts. *Ann. Otol. Rhinol. Laryngol.* **59**, 381–390.

NOGUCHI S., NOGUCHI A. and MURAKAMI N. (1970a) Papillary carcinomas of the thyroid. I. Developing pattern of metastasis. *Cancer* **26**, 1053–1060.

NOGUCHI S., NOGUCHI A. and MURAKAMI N. (1970b) Papillary carcinoma of the thyroid. II. Value of prophylactic lymph node excision. *Cancer* **26**, 1061–1064.

NUTTAL F. Q. (1965) Cystic metastases from papillary adenocarcinoma of the thyroid with comments concerning carcinoma associated with thyroglossal remnants. *Am. J. Surg.* **109**, 500–505.

O'KANE C. R. and STRAUS F. H. (1953) Papillary adenocarcinoma arising in association with a persistent thyroglossal duct. *Ann. Surg.* **138**, 805–806.

OWEN H. R. and INGELSBY H. (1927) Carcinoma of thyroglossal duct. *Ann. Surg.* **85**, 132–136.

POWELL L. W., BYERS T. F. and SCIORTINO A. (1965) Thyroglossal duct carcinoma. *Arch. Otolaryngol.* **82**, 189–190.

PAGE C. P., KEMMERER W. T., HAFF R. C. and MAZZAFERRI E. L. (1974) Thyroid carcinoma arising in thyroglossal ducts. *Ann. Surg.* **180**, 799–803.

REES C. E. and BROWN M. J. (1953) Cysts of the thyroglossal duct. *Am. J. Surg.* **85**, 597–599.

RUPPMANN E. and GEORGSSON G. (1966) Squamous carcinoma of thyroglossal duct. *Ger. Med. Mon.* **11**, 442–447.

SHEPARD G. H. and ROSENFELD L. (1968) Carcinoma of thyroglossal duct remnants. *Am. J. Surg.* **116**, 125–129.

SISTRUNK W. E. (1928) Technique of removal of cysts and sinuses of the thyroglossal duct. *Surg. Gynecol. Obstet.* **46**, 109–112.

SNEDECOR P. A. and GROSHONG L. E. (1965) Carcinoma of the thyroglossal duct. *Surgery* **58**, 969–978.

TANAKE K. and CINN W. H. (1963) Cancer arising in thyroglossal duct remnant. *Arch. Surg.* **86**, 466–477.

THOMAS C. G. jun. (1971) Thyroid cancer. In: WERNER S. C. and INGBAR S. H. (ed.) *The Thyroid*, 3rd ed. London, Harper & Row, p. 456.

VERONESI U., GENNAIR L. and CASCINELLI N. (1964) Carcinoma papillifero insorto su cisti del dotto tireglosso. *Tumori* **50**, 317–321.

WARD G. E., HENDRICK J. W. and CHAMBERS R. G. (1949) Thyroglossal tract abnormalities, cysts and fistulae. *Surg. Gynecol. Obstet.* **89**, 727–734.

WEBER A. O. (1968) Carcinoma of thyroglossal duct. *Calif. Med.* **108**, 127–130.

ZAMRAZIL V. NĚMEC J., PROKS C., NIEDERLE B., MANAK J. and ZEMAN K. (1971) Primary carcinoma of the thyroglossal duct treated by radio-iodine. *Neoplasma* **18**, 421–426.

Br. J. Surg. Vol. 62 (1975) 692–693

Secondary carcinoma of the thyroid gland

JOHN A. THOMSON, J. S. KENNEDY, M. K. BROWNE AND J. HUTCHISON*

SUMMARY

Two patients are described who presented with clinically solitary thyroid nodules which were found to be due to metastatic disease from the kidney and colon respectively. Removal of the solitary metastatis in one patient resulted in disease-free survival for over 5 years.

THERE has been considerable interest for some years in the clinically solitary thyroid nodule and the possibility of it being the site of a thyroid tumour. The likelihood of the thyroid being the site of a solitary metastasis has been much less commonly reported. The purpose of this communication is to document 2 such cases.

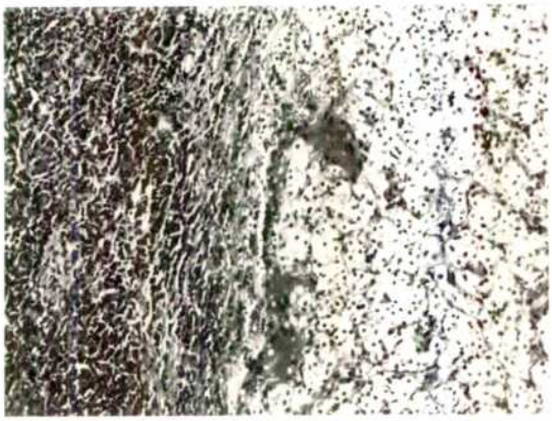


Fig. 1. *Case* 1. Secondary clear cell carcinoma of the kidney in the thyroid which shows chronic thyroiditis of Hashimoto type. HE. (×112.)

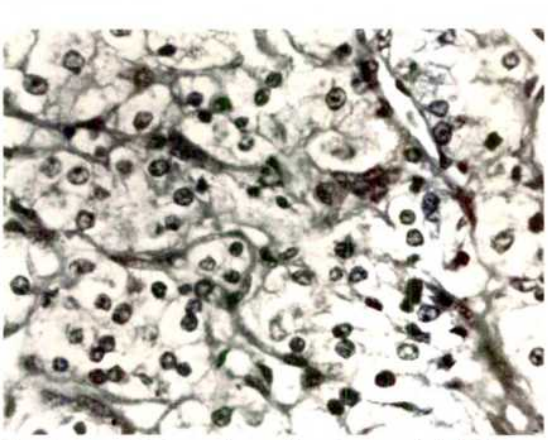


Fig. 2. *Case* 1. Primary clear cell carcinoma of the kidney. HE. (×450.)

Case reports

Case 1: A. O., a female aged 74 years, had a past history of carcinoma of the uterine cervix which had been treated by hysterectomy at the age of 58 years; there had been no subsequent symptomatology.

The patient presented to Glasgow Royal Infirmary when aged 63 because of left renal colic and haematuria. Investigation showed a non-functioning left kidney, and a left nephrectomy was performed in October 1963. A clear cell carcinoma of the kidney with no evidence of vascular invasion was found and there was no evidence of metastatic disease of the liver or the peritoneum at the time of operation.

In 1964 she was first noted to have a nodule in the region of the thyroid gland, but this was asymptomatic and was not further investigated. In 1969 she was referred back by her general practitioner because of enlargement of the thyroid nodule and the onset of some pressure symptoms. At that time she was clinically euthyroid and a cystic nodule of the right lobe of the thyroid displacing the trachea to the left was noted on examination. Thyroidectomy was performed in October 1969 and, as shown in *Fig.* 1, the appearance of the resected thyroid showed the presence of metastatic tumour of clear cell type in a gland showing thyroiditis of Hashimoto type. For comparison *Fig.* 2 shows the primary clear cell carcinoma of kidney removed in 1963. Following the operation the patient was treated by thyroxine therapy and has remained alive and well without any signs of recurrence of tumour.

Case 2: M. S., a female aged 44 years, presented in 1967 to Glasgow Royal Infirmary with a history of exertional dyspnoea and effort angina. She also complained of menorrhagia. A hypochromic anaemia of 7 g was diagnosed and she was treated with oral iron with improvement but relapsed the following year when she had a hypochromic anaemia of 5·4 g. A barium meal examination was negative and she was again treated with oral iron. In 1969 she was re-investigated because of recurrent anaemia, and at that time a vague mass was palpable in the right side of the abdomen. Barium meal and enema studies and intravenous pyelography were all normal, but at laparotomy she was found to have a carcinoma of the hepatic flexure of colon. This was treated by a right hemicolectomy. At operation there was no obvious metastatic disease but there was local invasion at the site of operation.

In September 1973 the patient was referred to the Thyroid Clinic at Glasgow Royal Infirmary with 4-month history of a thyroid nodule. She was euthyroid and on examination had a clinically solitary nodule of the isthmus of the thyroid gland. This was hard in consistency and was thought on clinical grounds to be malignant. There were no clinical features of metastatic disease but chest X-ray showed a small shadow in the left lung field. Tests of thyroid function were in the euthyroid range. The thyroid nodule was cold on scanning with radioactive iodine.

A preoperative diagnosis of thyroid malignancy was therefore made, and in view of the history of previous bowel surgery the possibility of this being metastatic was strongly considered. It was decided to explore the neck as this might show metastatic tumour, thus confirming the initial diagnosis; alternatively a primary thyroid carcinoma requiring treatment in its own right might be found. Accordingly, the neck was explored in October 1973 and the nodule of the isthmus removed. As shown in *Fig.* 3, this was found to be secondary tumour,

---

* Departments of Medicine, Pathology and Surgery, Glasgow Royal Infirmary.

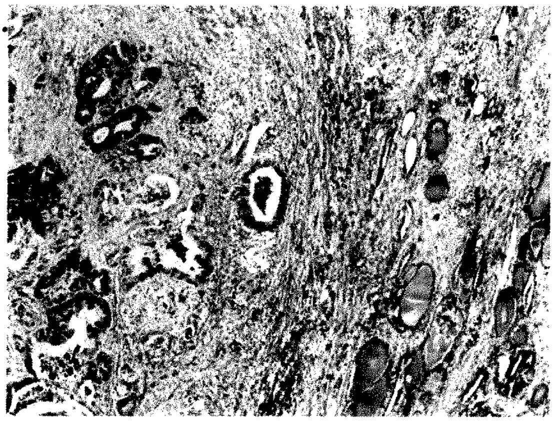


Fig. 3. *Case* 2. Secondary adenocarcinoma of the colon in the thyroid with abundant fibrous stroma. HE. (× 45.)

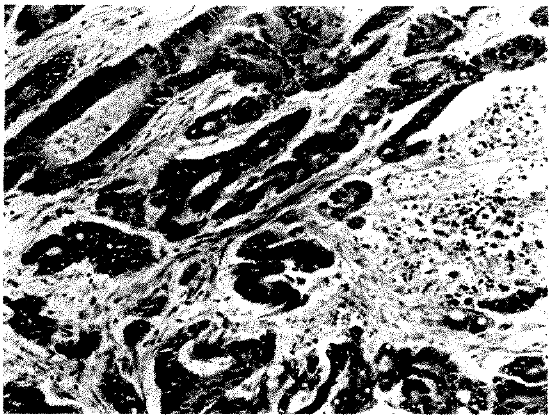


Fig. 4. *Case* 2. The primary tumour in the colon is a well-differentiated adenocarcinoma. HE. (× 112.)

invading the thyroid gland; the nature of the tumour was compatible with a colonic primary. For comparison a section of the original tumour is shown in *Fig.* 4.

Following thyroidectomy the patient was given a 5-day infusion of flurouracil. She remained well until March 1974 when she developed signs of cerebellar disease. Surgical exploration revealed secondary tumour in the cerebellum and hydrocephalus. Following resection of the metastatic tumour she improved temporarily but died 1 month later.

Discussion

Although secondary carcinoma of the thyroid gland has been recognized to occur as an infrequent finding it has been relatively disregarded even in major texts devoted to the thyroid. One of the few books on thyroid diseases which mentions the condition is that of Means et al. (1963), who amongst their list of recognized primary sources of tumour to metastasize to the thyroid include the two documented here, namely the kidney and the intestine. Recently, Gault et al. (1974) have recorded an example of clear cell renal carcinoma masquerading as thyroid enlargement, in this instance as a multinodular goitre, and reviewed the literature.

Metastatic tumours of the thyroid gland are of course seen in patients with very disseminated neoplasia, especially those from breast or bronchial carcinoma or from malignant melanoma. It should be emphasized, however, that in both the cases reported here the patient presented with a clinically solitary thyroid nodule in an otherwise fit patient, and it is worth while bearing in mind the possibility of metastatic thyroid disease in any patient who has had previous surgery for a malignant tumour and who subsequently presents with a solitary thyroid nodule. The experience of the first case led to the correct preoperative diagnosis being made in the second. The clinical course in *Case* 1 shows the value of resecting such an accessible solitary metastasis.

References

GAULT E. W., LEUNG T. W. H. and THOMAS D. F. (1974) Clear cell renal carcinoma masquerading as thyroid enlargement. *J. Pathol.* **113**, 21–25.

MEANS J. H., DEGROOT L. J. and STANBURY J. B. (1963) *The Thyroid and its Diseases*. New York. McGraw Hill, p. 506.

Br. J. Surg. Vol. 62 (1975) 694–696

The significance of occult skeletal metastases, detected by skeletal scintigraphy, in patients with otherwise apparently 'early' mammary carcinoma*

C. S. B. GALASKO†

SUMMARY

Fifty patients with apparently 'early' mammary carcinoma on clinical, radiological and biochemical grounds had a skeletal scintigram carried out when they first presented. Twelve (24 per cent) of the patients had a positive scintigram. All these patients have developed metastatic disease in the first 5 years following mastectomy, and at least 9 (75 per cent), and probably 10 (83 per cent), have died from mammary carcinoma during this period. This compares with 10 (26 per cent) of the patients with a negative scintigram who have developed recurrent or metastatic disease, of whom 8 (21 per cent) have died from their disease. Five years following mastectomy none of the patients with a positive scintigram was alive and free from disease, compared with 25 (66 per cent) of the patients with a negative scintigram.

It would appear that skeletal scintigraphy is the most sensitive method of detecting skeletal metastases and of staging breast carcinoma at the moment. Where practicable, this investigation should be carried out before embarking upon treatment for any particular patient, and this certainly should become part of any clinical trial comparing different therapeutic regimens. However, before some of the newer bone-seeking isotopes are used in this way, further studies are required to determine their false positive rate.

It is now well established that skeletal scintigraphy is more accurate and sensitive than conventional methods for the early detection of skeletal metastases (Galasko, 1972). It has also been shown that occult skeletal metastases are present on the scintigram in approximately 25 per cent of patients with apparently 'early' mammary carcinoma (Galasko, 1972). These studies did not show the significance of these occult lesions, or whether they affect the survival of the patients. An attempt to answer this question has been made by carefully following up 50 consecutive patients with apparently 'early' mammary carcinoma who had had a skeletal scintigram when they first presented.

Patients and methods

Fifty women with apparently 'early' mammary carcinoma were studied. Each patient had a careful clinical examination, a radiographic skeletal survey, an X-ray of her chest and biochemical liver function tests when she first presented. In addition, each patient had a skeletal scintigram. The method of scintigraphy has previously been reported (Galasko, 1969); ^{18}F and a gamma camera were used, and the scintigram was looked at in conjunction with the X-rays. All the investigations were carried out before treatment for the mammary carcinoma was instituted. All the patients had a mastectomy, either simple or radical, followed by a course of radiotherapy to the local lymph nodes. The patients have all been followed up for 5 years.

The results of the scintigram were ignored in determining treatment for the patients. If a patient developed other evidence of dissemination of her cancer, appropriate treatment was instituted.

Table I: OUTCOME IN 50 PATIENTS WITH APPARENTLY 'EARLY' MAMMARY CARCINOMA

	Scintigram positive		Scintigram negative		Total	
	No.	%	No.	%	No.	%
Number of patients	12	24	38	76	50	100
Subsequently developed disseminated cancer	12	100	10	26	22	44
Died from cancer	9 ?10	75 83*	8	21	17 ?18	34 36*
Died from intercurrent disease	0		3	8	3	6
Alive at 5 years	2	17	27	71	29	58
Alive with disseminated disease	2	17	2	5	4	8
Alive with no evidence of recurrence	0		25	66	25	50

* *See* text.

Results

In every patient the local tumour was thought to be operable. On the TNM classification it was T1 or T2, and in 2 patients with large breasts T3, by size. There was no fixity. The lymph nodes were either N0 or N1. Clinically, there was no evidence of dissemination of the disease. The radiographic skeletal survey, X-ray of the chest and liver function tests were entirely normal.

In 12 patients (24 per cent) lesions were found on the scintigram. In the remaining 38 (76 per cent) the scintigram was entirely normal (*Table I*). During the 5-year period all the patients with a positive scintigram developed metastatic disease, not only confirming the scintigraphic findings but usually involving other organs as well. During the same period 10 (26 per cent) of the patients with a negative scintigram developed either local recurrence or distant dissemination of their tumour.

---

* Based on a paper presented to the Surgical Research Society in July 1974.

† Department of Surgery, Royal Postgraduate Medical School, London.

Nine (75 per cent) of the patients with a positive scintigram have died from mammary carcinoma during the first 5 years. The tenth patient was lost to follow-up. Eighteen months following mastectomy, when she was desperately ill with hepatic and pulmonary metastases as well as skeletal metastases, she decided to return to Jamaica to die. If she is included in the deaths from mammary carcinoma the figure is 10 (83 per cent). This compares with 8 (21 per cent) of the patients with a negative scintigram who have died from mammary carcinoma during this period (*Table I*). None of the patients with a positive scintigram died from intercurrent disease. There were 3 such deaths (8 per cent) in the negative scintigram group. At autopsy in these patients there was no evidence of residual or metastatic tumour.

Two (17 per cent) of the patients with a positive scintigram were alive at 5 years but both had advanced mammary carcinoma. There were no patients in the positive scintigram group who were alive without evidence of recurrence at 5 years. In the negative scintigram group 27 (71 per cent) were alive at 5 years, 2 (5 per cent) of whom had metastatic disease. In this group 25 (66 per cent) patients were alive without evidence of recurrence at 5 years (*Table I*).

Discussion

The results of this study indicate that occult skeletal metastases detected by skeletal scintigraphy are significant and affect the patient's prognosis. There were no patients with a positive scintigram who were alive and free from disseminated disease at 5 years, compared with 66 per cent of patients with a negative scintigram. Twenty-six per cent of the patients with a negative scintigram developed metastatic disease and many of these developed skeletal metastases as well. These lesions were not detected by skeletal scintigraphy.

The results of the study also indicate that conventional methods of staging mammary carcinoma are grossly inaccurate. Using skeletal scintigraphy, approximately one-quarter of patients with otherwise apparently 'early' mammary carcinoma have occult skeletal metastases which severely affect their prognosis. Unfortunately, pulmonary and hepatic scintigraphy is not as accurate. Obviously the ideal would be some method of detecting tumour at all sites, be it primary or secondary, but until such a method becomes available, skeletal scintigraphy would appear to be the method of choice for staging mammary carcinoma, particularly in patients who are being admitted to a controlled clinical trial comparing different therapeutic regimens. Estimation of the carcino-embryonic antigen, α-feto protein, and other methods currently available are not sufficiently reliable for accurately staging apparently 'early' disease, although they may be very useful for assessing progress (Galasko, 1974)

In the present study there were no false positives on the skeletal scintigram. A localized increased concentration of bone-seeking isotopes is not specific for metastatic disease, and any condition which is associated with new bone production will show up as an area of increased concentration of the isotope (Galasko, 1973). Benign lesions, for example, Paget's disease of bone, osteo-arthritis, osteomyelitis with subperiosteal bone formation, fracture, etc., will be seen on the X-ray, as will primary malignant bone tumours. In this study a lesion was only reported if the X-ray was normal and there was no possible benign cause for the localized increased uptake of isotope. Where a benign lesion, which may be responsible for the uptake of isotope, was seen on the X-ray that particular area was regarded as normal for that patient. Using this method there were no false positives.

In recent years $^{99}Tc^{m}$-tagged pyrophosphate, polyphosphate and diphosphonate have become available for bone scanning. The technetium-tagged diphosphonate would appear to be the most suitable of these isotopes (Lavender, 1974; Tofe and Francis, 1974). ^{18}F is only available from the cyclotron or linear reactor and because of its short half life of 1·8 hours can only be used in fairly close proximity to the site of production. Technetium is much more readily available. Comparative studies between ^{18}F and $^{99}Tc^{m}$ diphosphonate indicate that the latter is probably more sensitive than the ^{18}F and may detect more and smaller metastases (Silberstein et al., 1973; Lavender, 1974). Because $^{99}Tc^{m}$ diphosphonate is so sensitive, very minor benign changes may show up as areas of localized increased uptake when no changes are seen on X-ray, and several false positives have been reported with technetium diphosphonate (Lavender, 1974). Before it comes into routine use for skeletal scintigraphy, and particularly for the staging of apparently 'early' mammary carcinoma, further studies are necessary to determine the false positive rate.

The results of this study also suggest that there may be three stages of mammary carcinoma: *early mammary carcinoma*, where there is no clinical, radiographic or scintigraphic evidence of dissemination of the disease, *early advanced disease*, where occult skeletal metastases are seen on the scintigram but there is no clinical or radiographic evidence of dissemination of the disease, and *advanced disease*, where metastases are obvious on clinical or radiographic examination. Clinical trials should compare separately patients in each subgroup. If patients with early advanced disease are excluded from clinical trials comparing different forms of local therapy, a significant difference may emerge between different forms of treatment.

The very interesting group would appear to be the patients with occult skeletal metastases. There is evidence which suggests that chemotherapy is most effective when the tumour deposits are still very small (Rowe-Jones, 1969). It is possible, therefore, that these patients should be treated by some form of adjuvant therapy as well as local excision of the primary tumour when they first present. Whether such adjuvant therapy will improve what is otherwise a very poor prognosis remains to be determined and could well be the subject of several controlled clinical trials.

References

GALASKO C. S. B. (1969) The detection of skeletal metastases from mammary cancer by gamma camera scintigraphy. *Br. J. Surg.* **56**, 757–764.

GALASKO C. S. B. (1972) Skeletal metastases and mammary cancer. *Ann. R. Coll. Surg. Engl.* **50**, 3–28.

GALASKO C. S. B. (1973) Skeletal scintigraphy. In: GILLILAND I. and PEDEN M. (ed.) *The Scientific Basis of Medicine. Annual Reviews, 1973*. London, Athlone, pp. 187–202.

GALASKO C. S. B. (1974) The early detection of recurrent and metastatic oncological disease. *Proc. R. Soc. Med.* **67**, 850–851.

LAVENDER P. (1974) Personal communication.

ROWE-JONES D. C. (1969) Cytotoxic penetration and concentration in human malignant tumours. *Br. J. Surg.* **56**, 774–778.

SILBERSTEIN E. B., SAENGER E. L., TOFE A. J., ALEXANDER G. W. jun. and PARK H. M. (1973) Imaging of bone metastases with ^{99m}Tc-Sn-EHDP (diphosphonate), ^{18}F and skeletal radiography. A comparison of sensitivity. *Radiology* **107**, 551–555.

TOFE A. J. and FRANCIS M. D. (1974) Optimization of the ratio of stannous tin: ethane-1-hydroxy-1, 1-diphosphonate for bone scanning with ^{99m}Tc-pertechnetate. *J. Nuc. Med.* **15**, 69–74.

the range is ours
the choice is yours

ETHICON
TRADEMARK
Eyeless needled sutures

REDUCE TRAUMA

ETHICON* Eyeless Needled Sutures offer three outstanding advantages over traditional eyed needles.

Point 1 Reduced trauma–with ETHICON eyeless needles there is no large eye and only one strand of material to pass through tissue.

Point 2 Consistent high quality–by precisely controlled manufacture of a complete sterile suture in a single package.

Point 3 A new sharp needle every time.

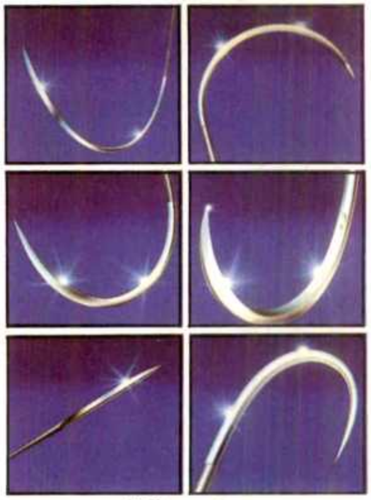
The choice is yours

Most surgeons agree that there is no universal suture. Most probably there never will be. Each patient, each procedure, and each layer of tissue differs from the next. This is why we at ETHICON manufacture such a comprehensive range of eyeless needled sutures.

You can choose from our wide selection of materials, absorbable and non-absorbable, securely attached to a stainless steel needle of your choice. The consistent high quality of ETHICON eyeless needled sutures provides predictable performance. This enables you to concentrate on the most critical aspect of your surgery–the well-being of the patient.

© ETHICON LTD 1974* Trade Mark

Quality and Reliability at every stage



We make some very important points

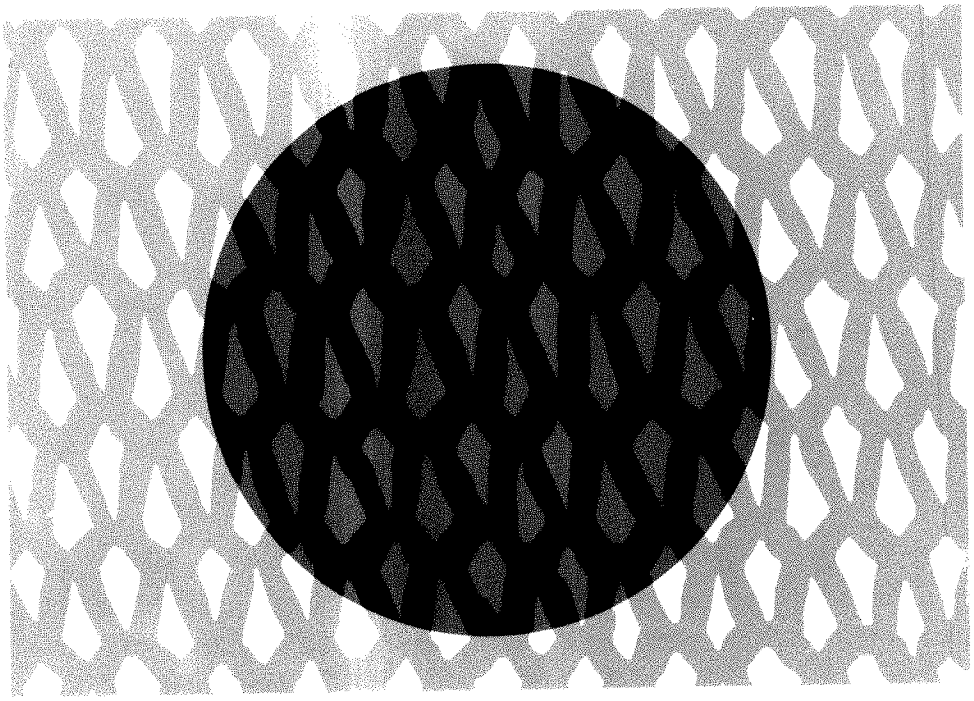
ETHICON
Eyeless needled sutures

Widest range. Finest quality

ETHICON Ltd., Bankhead Avenue, Edinburgh EH11 4HE, Scotland

SURGICEL*

Absorbable Haemostatic Gauze



instantly
controls
bleeding

ETHICON, LTD.

*Trademark ©ETHICON Ltd 1974

Br. J. Surg. Vol. 62 (1975) 697–700

Acute cholecystitis

P. A. M. RAINE AND A. A. GUNN*

SUMMARY

One hundred and fifty-six successive patients have been admitted with the clinical diagnosis of acute cholecystitis and have been treated by operation on the next operating list. The diagnosis was correct in 154 and a diagnostic pathway has been determined. The clinical features, investigations, bacteriology and pathology are discussed.

There is an increased need for choledochotomy in acute cholecystitis and this bile is more commonly infected than in the elective patient. It is suggested that those with infection can be identified prior to operation and should be treated with antibiotics on admission.

The morbidity of operation on patients with uninfected bile is no greater than in those receiving elective surgery, and operative treatment is recommended for both groups of patients.

THE management of acute cholecystitis remains controversial. The proponents of conservative treatment record the difficulty in confirming the diagnosis, with an error rate of between 5 and 24 per cent (Essenhigh, 1966; Van der Linden and Sunzel, 1970). Emergency surgery is said to carry a higher risk, with spread of infection and increased technical difficulty, particularly in detecting stones in the common bile duct (Wenkert et al., 1969; Jersky, 1970). Surgical treatment is advocated to abolish symptoms by removing the source of infection, to avoid further attacks and to allow the patient to return to normal life at an early date (Sokhi and Longland, 1973). This form of treatment reduces the time spent in hospital and expedites return to work with decreased insurance claims (Payne, 1969).

A consecutive series of patients has received operative treatment on the next operating list, and the clinical, operative, bacteriological and pathological data were recorded in a prospective manner.

Patients

Between 1965 and 1973, 156 patients were admitted to one surgical unit with the clinical diagnosis of acute cholecystitis. Attempts were made to confirm the diagnosis and to correct any abnormalities in the general health of the patient before the operation. During the same period 421 patients were admitted from the waiting list for elective biliary surgery and formed a basis for comparison.

Clinical details (*Table I*)

The emergency group of patients showed an increase in the ratio of male to female patients and the mean age was greater despite the shorter duration of symptoms. The increased frequency of a history of jaundice and abnormal liver function tests indicated that the pathological process was more advanced.

The diagnosis was correct with two exceptions. Both of these patients had pain, jaundice and a leucocytosis; the first had a duodenal perforation with marked oedema of the lesser omentum, and the second was proved to have haemorrhage into an infected hepatic metastasis.

Abdominal X-rays showed stones in 25, a calcified gallbladder in 4, a soft tissue swelling in 4 and gas in the biliary tract in 9 patients. No abnormality diagnostic of biliary tract disease was seen in the remaining 131, although a number of films showed other signs indicative of pathology in the right hypochondrium.

Table I: CLINICAL FEATURES OF THE EMERGENCY AND ELECTIVE GROUPS

	Emergency	Elective
Sex ratio (female : male)	3 : 2	3 : 1
Mean age (yr)	57·6	55·2
Duration of symptoms (%)		
<1 yr	52·0	13·7
>5 yr	19·0	40·8
History of jaundice (%)	36·4	23·5
Abnormal liver function (%)	49·3	20·0
Positive straight X-ray (%)	27·3	16·0

Oral cholecystography is only of value in patients who are neither vomiting nor have become jaundiced; 87 patients had this investigation and in 70 contrast was not concentrated in the gallbladder. When there is no vomiting, pyloric stenosis, diarrhoea, malabsorption and impaired liver function, absence of opacification was interpreted as evidence of obstruction of the cystic duct.

Intravenous cholangiography is limited to patients with normal liver function and by difficulties of interpretation when the ducts are poorly opacified. Twenty-four patients had this examination; 15 showed a normal duct system without filling of the gallbladder, 6 had stones in the common duct and 3 had a dilated duct.

Liver function tests were abnormal in 75 patients which suggested an element of obstruction in the common bile duct and placed a limit on the use of diagnostic X-rays. The bilirubin was raised in 64 cases, the alkaline phosphatase in 41, SGPT in 19 and prothrombin ratio in 24 patients.

Operative treatment (*Table II*)

All the operations were performed within 5 days of admission and the duration of symptoms before admission varied from less than 24 hours to 9 days. Thirty-one per cent of the patients required choledochotomy compared with 12 per cent in the elective series. Operative cholangiography has proved to be effective in the emergency situation (*Table III*), although 13 patients did not have this investigation: 7 because they were admitted early in the series before the technique was routine, 3 for technical reasons and 1 patient was iodine sensitive. In 2 patients the stones were felt and the duct opened without prior cholangiography.

---

* Bangour General Hospital, West Lothian.

Table II: OPERATIVE TREATMENT OF THE EMERGENCY AND ELECTIVE GROUPS

Treatment	Emergency	Elective
Cholecystectomy	105	343
Cholecystectomy and choledochotomy	48	57
Choledochotomy	1	18
Additional procedures		
Sphincterotomy	6	9
Choledochoduodenostomy	1	16
Gastric operations	2	30

Table III: RESULTS OF OPERATIVE CHOLANGIOGRAPHY IN THE EMERGENCY GROUP

Result: Satisfactory cholangiogram	No. of cases: 139
Stones in the common bile duct	38
Unsatisfactory cholangiogram	2
Cholangiogram not attempted	13

Table IV: INCIDENCE OF PYREXIA AND LEUCOCYTOSIS IN THE EMERGENCY GROUP IN PATIENTS WITH ACUTE CHOLECYSTITIS COMPARED WITH THOSE WITH CHRONIC CHOLECYSTITIS

	Acute cholecystitis	Chronic cholecystitis
Pyrexia over 37 °C	32·2	15·8
Leucocytosis over 10 000	50·8	42·1
Pyrexia and leucocytosis	20·3	15·8
No pyrexia or leucocytosis	37·3	57·9

Results given as percentages.

Table V: POSTOPERATIVE COMPLICATIONS IN THE EMERGENCY AND ELECTIVE GROUPS

Complication	Emergency	Elective
Pulmonary atelectasis	56	40
Pulmonary embolus	1·9	1·2
Deep vein thrombosis	0·7	1·6
Wound haematoma	1·3	2·6
Wound infection	5·9	5·0
Disruption	1·3	2·1
Biliary fistula	1·3	0·9
Biliary peritonitis	2·6	0·2
Subphrenic abscess	1·9	1·4
Waltman Walter's syndrome	1·3	0·2
Bacteriogenic shock	2·6	0·2
Oliguria	1·3	0·7
Death	2·5	0·2

Results given as percentages.

It proved difficult to record in detail the technical problems encountered, but the degree of difficulty was indicated and was found to increase progressively after 7 days from the onset of symptoms.

Pathological and bacteriological findings

The pathologist reported acute cholecystitis in 9·3 per cent, acute and chronic cholecystitis in 67·4 per cent and chronic cholecystitis in 23·3 per cent. Although this appears paradoxical, patients presenting with acute right hypochondrial pain may have obstruction in the biliary tract with or without inflammation.

In these three groups of patients there was no difference in sex, age or duration of symptoms, but half of the patients with chronic cholecystitis had a history of jaundice compared with less than a third of the other patients. The proportion of patients undergoing oral cholecystography was similar in each group but half of those with chronic disease had a functioning gallbladder compared with 1 in 10 of the remainder.

Thirty-five per cent of the immediate surgery patients had positive culture results of the bile, gallbladder or stones compared with 19 per cent in the elective series. Positive culture was more frequent in the patients with acute or acute with chronic pathological changes.

An attempt was made to correlate the pathological findings with the presence of a pyrexia or leucocytosis but this proved of little value (*Table IV*).

Postoperative complications (*Table V*)

Postoperative complications were recorded prospectively and, in particular, an X-ray was taken of the chest on the third postoperative day. Fifty-eight per cent of the patients in the emergency and elective groups had at least one complication, but when the 'postoperative chest' was excluded the incidence was 19·5 per cent in the emergency group and 16 per cent in the elective group. However, the finding of a positive culture of the bile increased the incidence to over 30 per cent in both groups of patients.

The complications that were more frequent in the emergency patients were those associated with infection and leakage of bile. The mortality was 2·5 per cent in this series compared with 0·2 per cent in the elective operations in the same period. The 4 deaths were in patients aged over 60 years with symptoms for more than 6 days. Each patient had infected bile but the

Table VI: DETAILS OF THE PATIENTS WHO DIED IN THE EMERGENCY GROUP

Sex	Age	Duration of symptoms (d)	Pathology	Operation	Post-mortem findings
F	61	9	Acute cholecystitis	Cholecystectomy	Coronary atheroma, pyelonephritis, pulmonary congestion
F	68	6	Perforated empyema	Cholecystectomy, choledochotomy	Pulmonary emboli
M	70	8	Acute cholecystitis, biliary peritonitis	Cholecystectomy, choledochotomy	Massive cerebral infarction
F	60	6	Acute cholecystitis	Cholecystectomy, choledochotomy	Fatty infiltration of the heart

post-mortem failed to confirm this as the cause of death (*Table VI*).

Discussion

Diagnosis

There was no formal scheme for the diagnosis of acute cholecystitis and two errors were made. However, a diagnostic pathway can be determined from the information obtained and appears to be helpful in confirming the clinical suspicion of acute biliary tract disorder if not of histological acute cholecystitis (*Fig.* 1).

Straight X-rays reveal the presence of biliary disease in 25 per cent but do not exclude other causes of pain such as acute pancreatitis. In the remainder jaundice suggests biliary tract disease and the liver function tests identify its obstructive nature. The presence of abnormal liver function tests limits the use of oral and intravenous cholangiography, and in such patients percutaneous transhepatic cholangiography is potentially dangerous. Retrograde cholangiography could have a place where the cause of the jaundice is in doubt, but in the majority laparotomy is essential and operative cholangiography permits accurate evaluation.

If the straight X-rays are negative and the patient is not jaundiced, cholecystography by the oral route is possible unless the patient is vomiting, when intravenous cholangiography is preferred. The oral cholecystogram may fail to reveal any filling of the gallbladder, and an intravenous cholangiogram would be necessary if there was reasonable doubt of the diagnosis.

In this series 15 patients without jaundice and with a negative straight X-ray had no further investigation and the decision to operate for acute cholecystitis was made on clinical grounds alone. A further 23 patients with a non-functioning gallbladder were treated by operation without an intravenous cholangiogram as suggested above.

Clinical judgement varies and it is suggested that the diagnostic pathway should be followed to provide further evidence of acute cholecystitis.

Infection

Various studies have suggested that infection is important in the mortality and morbidity of biliary operations (Haw and Gunn, 1973; Keighly and Graham, 1973). Infection in the bile was more common in the emergency series, as was the need for choledochotomy, and these facts may explain the higher mortality. However, where infection was not proved the morbidity and mortality were the same in both groups.

Certain criteria have been shown to be associated with an increased incidence of positive bile culture (Haw and Gunn, 1973), and if the diagnosis can be made the patient should receive appropriate antibiotic therapy prior to having the source of the infection removed. An analogy can be drawn with the treatment of acute appendicitis.

In the other patients where infection is considered unlikely there is no evidence of increased morbidity following operation, which is straightforward. If competent surgeons are available it is suggested that these patients should be treated by operation; but, if so decided, they could be treated conservatively with close observation.

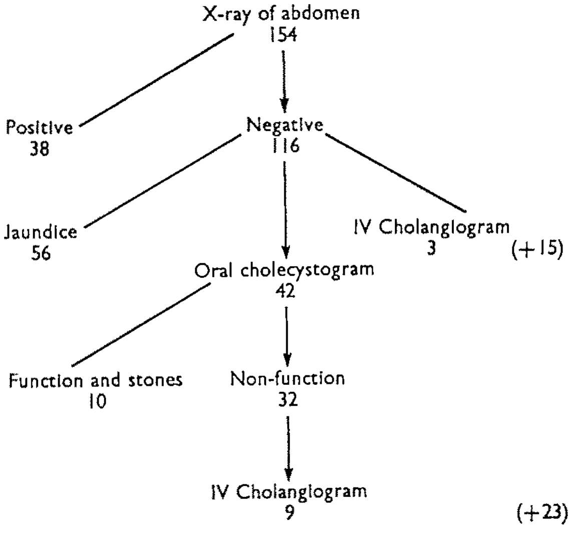


Fig. 1. The diagnostic pathway in the present series.

Conclusions

1. A diagnosis of cholecystitis can be reached in nearly every patient admitted as an emergency with 'acute cholecystitis', although in 25 per cent the pathology is chronic cholecystitis with no evidence of acute inflammation.
2. The operative mortality in patients with 'acute' cholecystitis is higher than in elective operations, but the former is a different group of patients with a higher incidence of infection and of stones in the common duct.
3. It is argued that the best treatment for a patient with 'acute' cholecystitis with a calculated risk of infection is to prescribe medical treatment including antibiotics and to operate within a few days. The exception would be in patients with symptoms of acute cholecystitis for more than 1 week when it is known that the technical difficulties increase.
4. Patients with 'acute' cholecystitis without a calculated risk of infection can be safely treated by operation.
5. In conclusion it is necessary to emphasize that surgery on a tense inflamed gallbladder requires technical competence and experience.

References

ESSENHIGH D. M. (1966) Management of acute cholecystitis. *Br. J. Surg.* **53**, 1032–1038.

HAW C. S. and GUNN A. A. (1973) The significance of infection in biliary disease. *J. R. Coll. Surg. Edinb.* **18**, 209–212.

JERSKY J. (1970) The management of acute cholecystitis. *S. Afr. J. Surg.* **8**, 41–45.

KEIGHLEY M. R. B. and GRAHAM N. G. (1973) Infective cholecystitis. *J.R. Coll. Surg. Edinb.* **18**, 213–220.

PAYNE R. A. (1969) Evaluation of the management of acute cholecystitis. *Br. J. Surg.* **56**, 200–203.

SOKHI G. S. and LONGLAND C. J. (1973) Early and delayed operation in acute gall-stone disease. *Br. J. Surg.* **60**, 937–939.

VAN DER LINDEN W. AND SUNZEL H. (1970) Early versus delayed operation for acute cholecystitis. *Am. J. Surg.* **120**, 7–13.

WENKERT A. and HALLGREN T. (1969) Evaluation of conservative treatment of acute cholecystitis. *Acta Chir. Scand.* **135**, 701–706

IN accordance with the underlying pathologic principles, surgical treatment may be directed toward removing or destroying the bleeding varix, reducing so far as possible the amount of blood entering the portal circulation or increasing the collateral channels to such an extent that the portal hypertension and stasis will be relieved. While the first is not altogether a surgical impossibility, it would be a decidedly dangerous procedure. Cauterization of the varices through the esophagoscope is the only method by which it has been attempted, and so far this has met with little success. Another method of attack would be to ligate the coronary vein or group of veins between the cardia and the trunk of the portal vein, but the feasibility of this procedure is open to question. The second possibility, that of reducing the amount of blood entering the portal circulation, involves removal of the spleen, which contributes about 20 per cent of the total portal stream. This has already given good results in selected cases.

Considering that the whole tendency of portal cirrhosis is to divert the stream of portal blood away from the liver, leaving the arterial blood to provide for the parenchymal requirements, the most logical and effective method of dealing radically with the embarrassed portal circulation would doubtless be to perform a simple Eck fistula. By this means the portal hypertension would be relieved, stasis immediately abolished, and the development of varices arrested. The ideal procedure would be side-to-side anastomosis of the portal vein and inferior vena cava without ligating any trunks. This would not interfere with any other blood already reaching the liver. Although Eck fistulas have been tried at various times, the resultant uniform failure seems to be entirely due to difficulties in the operation itself. Provided a satisfactory technic can be evolved, such as that employed by Mann and his associates in their experimental work with Eck fistula on dogs, there is no reason why in suitable cases it should not be successful.

ARCHIBALD H. McINDOE (1928) Vascular lesions of portal cirrhosis. *Arch. Pathol. Lab. Med.* **5**, 23–42.

Br. J. Surg. Vol. 62 (1975) 701–706

Prognosis after portocaval anastomosis: a 15-year follow-up

R. WINDLE AND J. H. PEACOCK*

SUMMARY

A 15-year follow-up of 57 patients who underwent portocaval anastomosis is reported. Twenty-seven patients were still alive and the progress of these and of those who died is followed.

The young cryptogenic cirrhotic with no encephalopathy, normal liver function tests and absence of portal vein mural thrombus at the time of operation is best benefited.

The only factor from the series to suggest a poor prognosis is deterioration in liver function in the post-jaundice cirrhotic, and the development of encephalopathy in cryptogenic cirrhotics suggests a poor long term prognosis, but its onset is not related to the time before death.

CIRRHOSIS, by distortion of the intrahepatic portal vascular bed, gives rise to portal hypertension, and the portal flow through the liver is reduced to 13 per cent (McIndoe, 1928); the rest bypasses the liver along natural portal-systemic anastomoses, one existing in the lower oesophagus between branches of the left gastric vein and those of the azygos, intercostal and diaphragmatic veins. Haemorrhage from varicosities in these veins in the oesophageal wall in portal hypertension accelerates death in 30 per cent of cirrhotics (Truelove, 1972), and the immediate mortality of bleeding has been stated to be as high as 54 per cent (Hislop et al., 1966).

Portocaval anastomosis should relieve the portal hypertension with usually minimal but unpredictable deterioration in hepatic function, depending on the reduction in hepatic blood flow following the operation (Nardi, 1955; McDermott, 1965).

Portocaval anastomosis has been performed in Bristol for intrahepatic portal obstruction since 1950. This report is concerned with the patients in whom the operation was performed more than 15 years ago in order to ascertain the late effectiveness of anastomosis in stopping bleeding and the resultant side effects.

Patients

During the period 1950–7, 57 patients underwent end-to-side anastomosis of the portal vein to the inferior vena cava at Bristol Royal Infirmary for portal hypertension secondary to intrahepatic disease. Virtually all had experienced one or more severe haematemeses, 2 patients had asymptomatic varices and another had presented with associated iron deficiency anaemia. All had been shown to have oesophageal varices on barium swallow studies or oesophagoscopy, and after 1952 the patency of the portal vein was demonstrated by percutaneous splenoportography (Walker et al., 1953), and in those who had previously had a splenectomy by operative portal venography.

The aetiology of the liver disease in the majority was unknown (*Table I*). There were 35 males and 22 females, their ages ranging from 7 to 57 years (average 33 years) at the time of operation (*Fig*. 1).

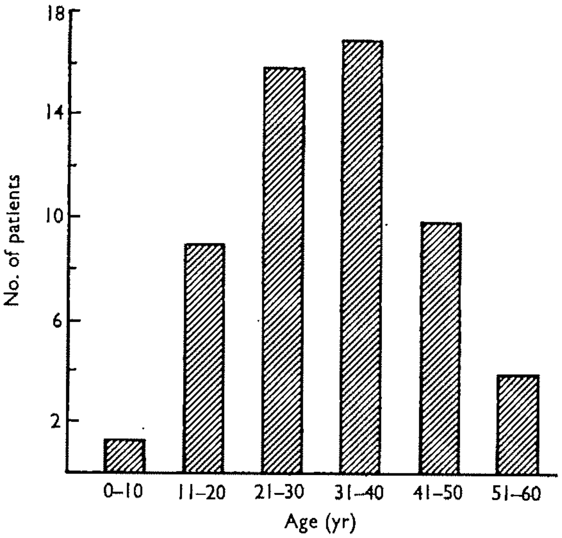


Fig. 1. Age at operation.

Table I: AETIOLOGY OF THE CIRRHOSIS

Aetiology:	No. of cases:
Unknown (cryptogenic)	38
Post-jaundice	9
Alcoholic	6
Bilharzia	1
Wilson's disease	1
Primary portal fibrosis	2
Total	57

Selection of patients for operation was on age—all the patients submitted to operation being under 60 years of age—the absence of clinical jaundice and a serum albumin of greater than 3 g/100 ml, regardless of other biochemical data.

The operative technique has been described (Walker, 1959); operative saline manometry of the portal vein pressure was performed, and if intraportal mural thrombus was found it was removed unless endothelialized and the lumen adequate.

---

* Department of Surgery, Royal Infirmary, Bristol.
Present address of R. Windle: The Radcliffe Infirmary, Oxford.

Table II: OUTCOME IN PATIENTS WITH THROMBUS IN THE PORTAL VEIN

Outcome	No. of cases	
Thrombus in portal vein at operation		10
Thrombus excised		8
Non-survivors		7
Hepatic failure, patent shunt	3	
Haemorrhage and coma, thombosed shunt	1	
Unrelated cause, thrombosed shunt	3	
Survivors		3
No further haemorrhage	2	
Recurrent haemorrhage	1	

Table III: AVERAGE AGE AT OPERATION

Aetiology	Age (yr) Survivors	Non-survivors
Total	26·7	36·8
Cryptogenic group	27·8	38·5
Post-jaundice group		39·5

Table IV: CAUSE OF DEATH IN OPERATIVE SURVIVORS

Cause of death:	No. of cases:
Hepatic failure	17
Recurrent haemorrhage	2
Unrelated	6

Table V: GRADE OF SEVERITY OF POSTOPERATIVE SYMPTOMS AT 15 YEARS

Grade	Total no. of cases	Cryptogenic group	Alcoholic group
Symptoms: None Bleeding: None Work: Full	17	16	1
Symptoms: Minimal Bleeding: None Work: Full Occasional visits to doctor	5	4	1
Symptoms: Troublesome Repeated visits to doctor Occasional hospital admissions Work: On and off	2	1	1
Symptoms: Severe Work: None No liver failure	1	1	0

Table VI: FURTHER HAEMORRHAGE

Cause	No. surviving	Fatal haemorrhage
Recurrent varices ± shunt thrombosis	2	2*
Peptic ulcer	2	1
Unknown	1	

* One operative death.

Table VII: OUTCOME IN PATIENTS WITH PEPTIC ULCERATION

Outcome:	No. of cases:
Clinically healed no treatment	2
Radiologically healed no treatment	2
Healed after vagotomy and drainage	2
Fatal haemorrhage	2*
Total	8

* One died at 18 years.

Results

Four patients died in hospital in the postoperative period, an operative mortality of 7 per cent. Three of these patients died from hepatic failure and the remaining patient, in whom thrombus had been removed from the portal vein at operation, developed thrombosis of the shunt and died from further haemorrhage.

Ten patients had thrombus in the portal vein at operation (*Table II*); 4 of these developed proved shunt thrombosis and another patient had probable shunt thrombosis during the period of follow-up.

Twenty-five patients have subsequently died and one is untraceable, leaving 27 patients alive at 15 years (48·2 per cent). Of these, a further 5 have died between 15 and 20 years (2 of liver failure and one each from myocardial infarction, bleeding peptic ulcer and nephrotic syndrome) and are counted alive in this series. Four patients are alive and perfectly well at 21 years. The age of the survivors at operation was 10·1 years younger than that of the non-survivors (*Table III*).

Preoperatively the average serum bilirubin levels of the operative non-survivors, 15-year non-survivors and 15-year survivors were 0·5, 0·7 and 0·5 mg/100 ml respectively. One patient who was alive at 15 years had a level raised above normal preoperatively, but 8 patients who died within 15 years of the operation had abnormally raised serum bilirubin levels. Average serum alkaline phosphatase levels were 18 King Armstrong units/100 ml for the group of operative non-survivors, 14·5 King Armstrong units/100 ml for the group of 15-year non-survivors and 11·5 King Armstrong units/100 ml for the group of 15-year survivors. Four patients in the last group had abnormally raised levels preoperatively, whereas 7 in the group of patients not surviving to 15 years had abnormally raised levels. As stated before, all the patients had serum albumin levels greater than 3 g/100 ml and there was no significant difference in the albumin levels of the three groups.

In 68 per cent of the non-survivors the cause of death was hepatic failure (*Table IV*). Portal-systemic encephalopathy has occurred in 21 of the operative survivors (38 per cent), 13 having since died, but only 2 of these 13 were unable to work after the operation. Only patients over the age of 30 years at the time of operation were affected by encephalopathy prior to their terminal illness. At the time of follow-up 2 were unable to work due to encephalopathy; the other 6 had experienced mild bouts but 3 of them were totally free of encephalopathy when seen (*Table V*). Ten patients (19 per cent) developed encephalopathy within 5 years of the operation, and a further 8 did so in the next 5 years. Unfortunately many of the patients were given high protein diets during the early postoperative phase. This was revised when it became known that such diets predisposed the patients to portal-systemic encephalopathy.

Further haemorrhage has occurred in 8 patients, causing 1 operative and 2 later deaths (*Table VI*). The 2 patients who survived bleeding from recurrent varices had both undergone splenectomy prior to the shunt and were treated by oesophageal transection. Neither has bled since and one has no demonstrable varices at 15 years. One non-survivor had asymptomatic varices demonstrated at autopsy. Seventeen of the survivors who had not had further haemorrhage have been checked radiologically or by oesophagoscopy for varices, which have been found in 2.

Peptic ulceration has been demonstrated in 8 patients, of whom 2 had ulcers preoperatively, giving a post-shunt incidence of 12 per cent (*Table VII*).

Five patients have developed diabetes mellitus and 2 haemochromatosis since operation. No operative survivors had any significant anaemia, neutropenia or thrombocytopenia.

Considering the results in each aetiological group, 22 of the 34 patients with cryptogenic cirrhosis who survived the postoperative period (64 per cent) were alive at 15 years. Eight died of hepatic failure, their liver function deteriorating as shown in *Figs.* 2 and 3, and one each of respiratory complications, pyosalpinx, peptic ulcer haemorrhage and cardiac failure. The deaths were evenly distributed over the 15 years since operation (*Figs.* 4, 5), and their relationship to the age at operation is shown in *Table VIII*.

Ten of these non-survivors had experienced bouts of encephalopathy but all but 2 had been able to work after the operation. Of the 22 survivors with cryptogenic cirrhosis, all but one (with gross encephalopathy) were working at 15 years (*Table V*), 2 had mild encephalopathy but a total of 16 had experienced no postoperative encephalopathy. Of these 22 patients, the liver function tests showed no change after operation in 9, deterioration with subsequent recovery in 6 and deterioration without remission in 5 (*Figs.* 2, 3); there was insufficient data on the remaining 2.

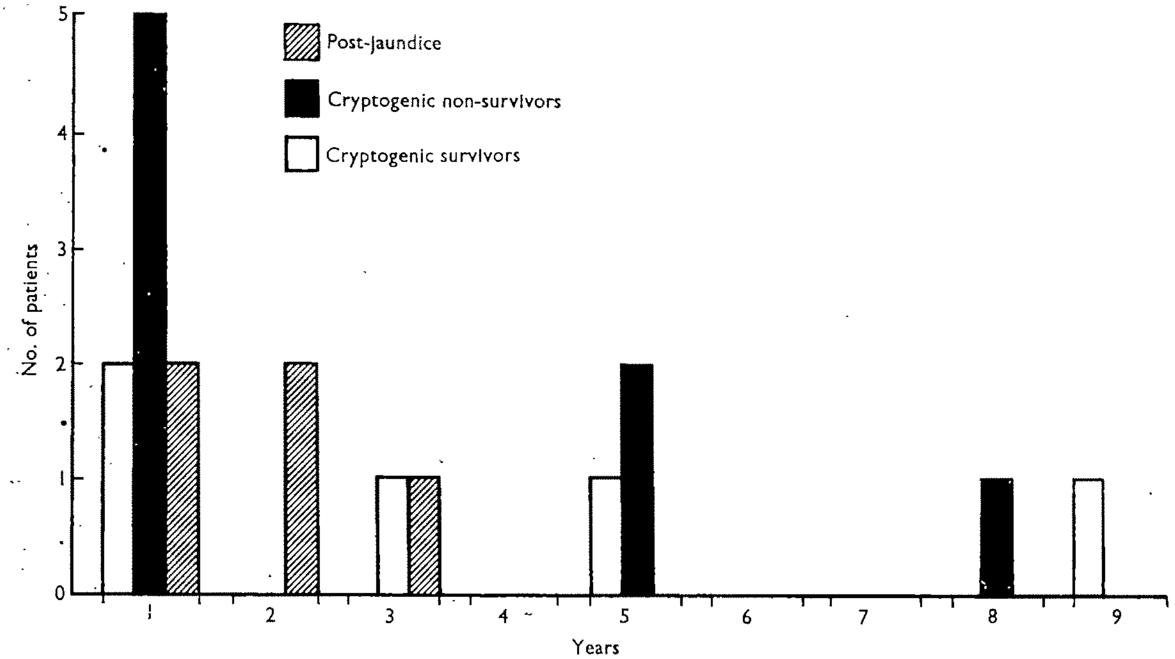


Fig. 2. Time between onset of irreversible liver decompensation and death or time of follow-up.

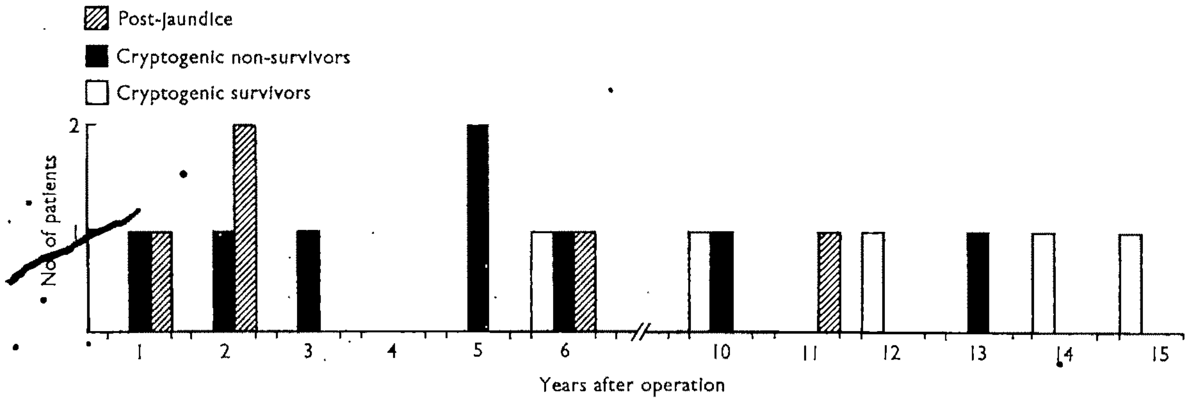


Fig. 3. Time between operation and onset of liver decompensation.

All 9 patients with a history of jaundice prior to their cirrhosis were dead by 13 years (*Fig.* 4). At operation they were between 19 and 55 years old (average 39·5). Five patients died of liver failure, and the others of bleeding varices, aortic aneurysm, carcinoma of the pancreas and suicide. The relationship of survival to age at the time of operation is shown in *Table VIII*, and the relationship of liver failure to the operation and to subsequent death in *Figs.* 2 and 3. Only 2 patients had encephalopathy at any time prior to the terminal illness and 6 patients could work after their operation.

Six patients had a history of excessive alcohol intake. One was untraceable, one died of liver failure in the first year and one continued drinking and died of liver failure in the third year after operation. Three are still alive; one now incapacitated by encephalopathy, one having mild encephalopathy and fluctuating liver function tests which were normal at the time of follow-up and one with neither encephalopathy nor liver decompensation (*Table V*). The latter 2 still appear to be drinking alcohol.

The patient with bilharzia had normal liver function at 15 years but was developing nephrotic syndrome (from which he has since died). One patient with Wilson's disease died of liver failure at 3 years, and of the 2 with portal fibrosis, one died at 6 years after operation and the other is alive and well.

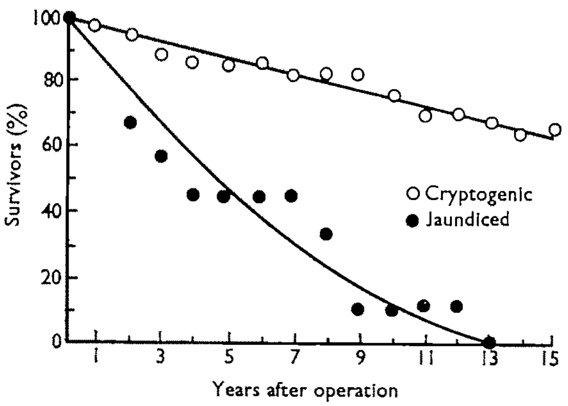


Fig. 4. Proportion of operative survivors against time.

Discussion

Without operative intervention, up to 63 per cent of adults bleeding from oesophageal varices will bleed again during the first year of follow-up (Sherlock, 1964). In 15 years of follow-up, 4 (7 per cent) of our patients have had further bleeding owing to recurrent varices after the shunt operation. Of the 4, 2 have been controlled by further surgery to the oesophagus. Forty-eight had no recurrent haemorrhage, and of these, 40 came to autopsy or were investigated to see whether they had recurrence of oesophageal varices. These were found in 3 patients, giving a total recurrence rate of 12 per cent in the 48 patients investigated.

The problems that portocaval anastomosis creates for the patient are well known. Other than an increase in the burden of hepatic decompensation, portosystemic encephalopathy, diabetes mellitus and peptic ulceration as well as other less common problems including haemosiderosis and pulmonary complications can occur (Grace and Balint, 1966; Sherlock et al., 1970). The operative mortality of 7 per cent in this series is within that quoted by Sherlock (1971) of 5 per cent and by Hunt (1967) of 8 per cent for elective portocaval anastomosis, in distinction to the much higher figure of 25 per cent (Sherlock, 1971) for emergency portocaval anastomosis.

Portal-systemic encephalopathy, widely quoted as the major limiting factor in the success of portocaval anastomosis, occurs in as many as 48 per cent of patients to a measurable degree (Sherlock et al., 1970)

Table VIII: RELATIONSHIP OF SURVIVAL TO AGE AT OPERATION

	Age at operation (yr)				
Group	11–20	21–30	31–40	41–50	51–60
Cryptogenic cirrhosis					
Total	5	13	13	5	2
No. alive at 5 yr	5	12	9	4	0
No. alive at 10 yr	5	12	9	3	0
No. alive at 15 yr	4	11	8	0	0
Post-jaundice cirrhosis					
Total	1	2	1	3	2
No. alive at 5 yr	0	2	0	1	1
No. alive at 10 yr	0	0	0	1	0
No. alive at 15 yr	0	0	0	0	0

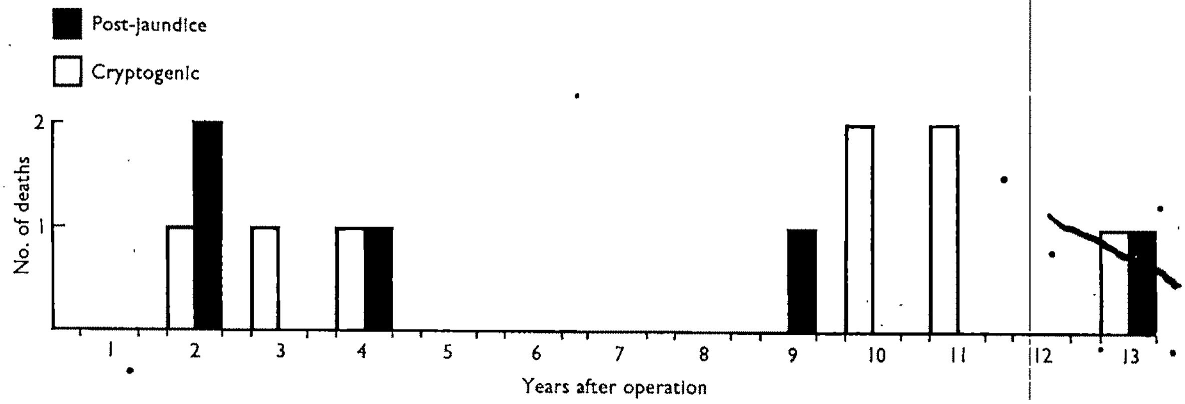


Fig. 5. Number of deaths of patients from hepatic failure per year after operation.

and to a severe degree in from 15 per cent (Grace et al., 1966) to 37 per cent (Read et al., 1961). Of the 53 operative survivors, 21 patients (38 per cent) developed portal-systemic encephalopathy, the onset being distributed over the 15 years following surgery, with a predominance during the first 5 postoperative years. However, only 4 (8 per cent) were persistently kept from working by it. Portal-systemic encephalopathy was a worse problem in the cryptogenic cirrhotic group, 47 per cent of which developed the complication, as opposed to the older post-jaundice cirrhotic group of which only 28 per cent developed encephalopathy prior to their terminal illness. This does not agree with our observation or that of others (Read et al., 1961) that portal-systemic encephalopathy occurs more often in higher age groups, and suggests that portal-systemic encephalopathy and liver biochemistry deterioration do not occur together in the post-jaundice group.

Sixty-eight per cent of our patients died of hepatic failure. Eight of the 34 patients with cryptogenic cirrhosis died of liver failure, with a further 5 showing deterioration of liver function. The onset of liver failure began at a variable period postoperatively but in 75 per cent it became manifest during the first 6 years. A greater proportion (5 out of 9) of post-jaundice cirrhotic patients died of hepatic failure, 60 per cent of them developing it within 2 years of the operation. This deterioration of liver function in the early years after portocaval anastomosis has been observed previously by Sherlock et al. (1970) and demonstrates what is often the progressive nature of cirrhosis following hepatitis.

In predicting the patients best benefited by portocaval anastomosis it is considered that the younger the patient and the less the hepatic decompensation, the better is the prognosis postoperatively, jaundice, low serum albumin and portal-systemic encephalopathy being contraindications to the operation (Sherlock, 1964). The young cryptogenic cirrhotic was best benefited in our series; 82 per cent of those under 30 years at operation were alive at 15 years, while none of the patients over 40 years at operation was alive at 15 years (*Table VIII*). The patients who had post-jaundice cirrhosis and who were of ages comparable to the non-surviving group of cryptogenic cirrhotics did no better, all dying by 13 years after the operation.

The patients with alcoholic cirrhosis, who usually progress well after the operation if drinking is stopped (Sherlock, 1971), did well in the small series we present here, 3 out of 5 patients being alive at 15 years and the 2 least incapacitated by encephalopathy still drinking alcohol. However, of 15 patients, all alcoholic cirrhotics, who have undergone portocaval anastomosis since 1957 in Bristol, 11 are traceable and 9 of these have died of liver failure within 5 years of operation.

Patients with any degree of liver decompensation are not usually submitted to elective portocaval anastomosis, and it can be seen from our series that the patients with an abnormally raised serum bilirubin level have not progressed as well as those with normal bilirubin levels. Abnormally raised alkaline phosphatase levels in the serum appear to be of less significance.

Patients who had thrombus in the portal vein at operation did not progress well after the operation; 30 per cent were alive at 15 years and 80 per cent of them had rethrombosis of the shunt. This even applied when the thrombus was easily removed from the portal vein at operation.

The progress of the patient after his portocaval anastomosis allowed some prediction of his ultimate prognosis. If the patient had further haemorrhage, whether this was associated with shunt thrombosis or with a peptic ulcer, the problem was serious and even haemorrhage from peptic ulcer had a mortality of 33 per cent. Deterioration in liver function heralded a rapid deterioration in the patients who had post-jaundice cirrhosis, and commonly, but not as often, in the patients with cryptogenic cirrhosis. However, portal-systemic encephalopathy had a prognostic significance only in the patients who had cryptogenic cirrhosis, as 10 of the 12 operative survivors in the latter group who were dead by 15 years had portal-systemic encephalopathy, but there was little relationship to time, as those with portal-systemic encephalopathy at 10 years were all alive at 15 years.

Acknowledgements

We acknowledge with gratitude the fact that these patients are the original series of Professor R. Milnes Walker (Walker et al., 1961).

We also acknowledge the help of Dr P. D. Mulcahy, Dr G. M. Colson, Dr J. N. MacCaig, Dr P. J. Toghill and Dr M. J. Whelton in tracing and arranging investigations on their patients included in this series.

References

Grace N. D. and Balint J. A. (1966) Haemochromatosis associated with end to side porto-caval anastomosis. *Am. J. Dig. Dis.*, **11**, 351–358.

Grace N. D., Muench H. and Chalmers T. C. (1966) The present status of shunts for portal hypertension in cirrhosis. *Gastroenterology* **50**, 685–691.

Hislop I. G., Waters T. E., Kellock T. D. and Swynnerton B. (1966) The natural history of haemorrhage from oesophageal varices. *Lancet* **1**, 945–948.

Hunt A. C. (1967) Observations on the treatment and prognosis of portal hypertension. In: Read A. E. (ed) *The Liver, Proceedings of the Nineteenth Symposium of the Colston Research Society, Bristol 1967.* London, Butterworths, pp. 371–375.

McDermott W. V. jun. (1965) The techniques of portal-systemic shunt surgery. *Surgery* **57**, 778–786.

McIndoe A. H. (1928) Vascular lesions of portal cirrhosis. *Arch. Pathol.* **5**, 23.

Nardi G. L. (1955) Effects of spleno-renal shunts on hepatic blood flow. *Arch. Surg.* **70**, 530–534.

Read A. E., Laidlaw J. and Sherlock S. (1961) Neuropsychiatric complications of porto-caval anastomosis. *Lancet* **1**, 961–963.

SHERLOCK S. (1964) Haematemesis in portal hypertension. *Br. J. Surg.* **51**, 746–749.

SHERLOCK S. (1971) *Diseases of the Liver and Biliary System*, 4th ed. Oxford, Blackwell, pp. 165–227.

SHERLOCK S., GEORGE P. and HOURIGAN K. (1970) Medical complications of shunt surgery for portal hypertension. *Ann. NY Acad. Sci.* **170**, 392–405.

TRUELOVE S. C. (1972) *Diseases of Digestive System*, 2nd ed. Oxford, Blackwell, pp. 608–613.

WALKER R. M. (1959) *Pathology and Management of Portal Hypertension*. London, Arnold, p. 67.

WALKER R. M., MIDDLEMISS J. H. and NANSON E. M. (1953) Portal venography by intra-splenic injection. *Br. J. Surg.* **40**, 392–395.

WALKER R. M., SHALDEN C. and VOWLES K. D. J. (1961) Late results of porto-caval anastomosis. *Lancet* **11**, 727–730.

Br. J. Surg. Vol. 62 (1975) 707–712

The effect of acute ethanol administration on the exocrine pancreatic secretion of the pig

I. C. WHEATLEY, G. O. BARBEZAT, ROSEMARY HICKMAN
AND J. TERBLANCHE*

SUMMARY

The acute effect of intravenous and intragastric alcohol on exocrine pancreatic secretion was studied in pigs with chronic pancreatic and gastric fistulas. A new H-type pancreatic cannula was designed for the study.

With intravenous alcohol and the gastric fistula open, increased gastric acid secretion occurred but pancreatic enzyme output was inhibited. When acid was allowed to enter the duodenum by closing the gastric fistula, intravenous alcohol produced a secretin-like effect of increased pancreatic volume and bicarbonate secretion.

Intragastric alcohol caused an increase in volume, bicarbonate and enzyme output. This was probably due initially to direct gastroduodenal stimulation as the same response occurred following intragastric mannitol of similar volume, pH and osmolality. The subsequently sustained increase in volume and bicarbonate was possibly a secondary secretin-like response following absorption of alcohol.

It is concluded that the pig pancreas responds to alcohol as has been described in other animals. The use of a single model has allowed clarification of various phases of response invoking the effects of secretin, gastric and glucagon.

ALCOHOL abuse is the commonest cause of pancreatitis in the Western Cape of South Africa (Marks et al., 1974). The exact pathogenesis is not known despite investigations in many laboratories and in a number of models (Dreiling et al., 1952; Davis and Pirola, 1966; Janowitz and Bayer, 1971). Some workers have found that alcohol stimulates pancreatic secretion (Lowenfels et al., 1968), but depression has also been noted (Bayer et al., 1972; Mott et al., 1972; Tiscornia et al., 1973). In some studies gastric secretion was diverted from the duodenum, while in others the important secondary effect of duodenal acidification and secretin release was retained (Walton et al., 1960). The present study was designed to determine the acute effect of intravenous and intragastric alcohol on secretin- and cholecystokinin-stimulated exocrine pancreatic secretion in a uniform porcine model. It constitutes a preliminary phase of a projected study of the effect of alcohol on the chronically damaged pig pancreas, using a model developed in our laboratory (Waterworth, Bank and Terblanche, 1973).

Materials and methods

A new cannula was developed to establish a chronic pancreatic fistula in the pig (Wheatley et al., 1974). This was H-shaped and made of Fluorodur, a synthetic biologically inert plastic material (*Fig.* 1). The vertical limbs of the H were 10 cm long with an internal diameter of 1 cm and a wall thickness of 5 mm. The cross-connection was 4 cm long. For collection of pancreatic juice an inner sleeve was inserted into the limb draining the pancreatic duct.

Studies were performed on Large White × Landrace female pigs weighing 20–35 kg. Operations were conducted under sterile conditions using thiopentone sodium for induction, and nitrous oxide, oxygen and halothane for maintenance of general anaesthesia.

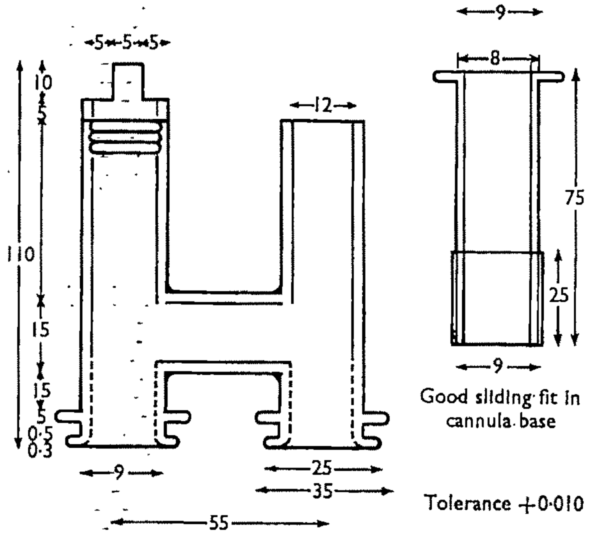


Fig. 1. Specification for manufacture of the H-shaped cannula from Fluorodur. (Lengths in mm.)

The pancreatic duct in the pig enters the medial wall of the duodenum 7–10 cm distal to both the pylorus and the common bile duct. This portion of the duodenum was divided at 3 cm on either side of the pancreatic duct and a pouch constructed by closing both ends of the free segment of duodenum. Duodenal continuity was restored by end-to-end anastomosis. One limb of the cannula was inserted into the pouch opposite the pancreatic duct, and the other limb into the duodenum proximal to the anastomosis. The

---

* Departments of Surgery and Medicine, University of Cape Town Medical School, South Africa.
Reprint requests to Dr R. Hickman, Department of Surgery, University of Cape Town Medical School, Observatory, Cape, South Africa.

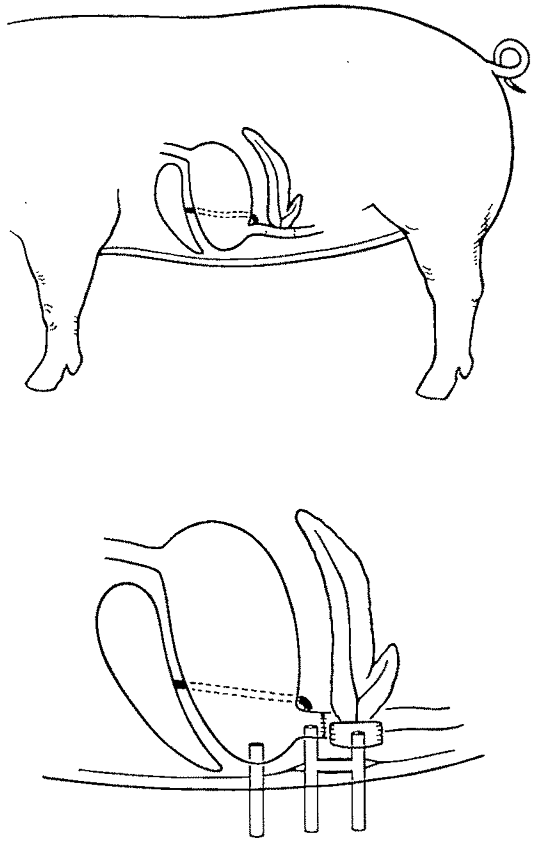


Fig. 2. Diagram showing the pancreatic and gastric cannulas in position.

cannula was retained with a purse string suture and several interrupted silk sutures holding the surrounding duodenal wall to the outer flange. Omentum was wrapped liberally around the inner ends of the cannula. The outer ends of the cannula were then brought out through the anterior abdominal wall to the right of the midline. The peritoneum was resutured deep to the cross-piece in order to retain this extraperitoneally. A gastric cannula was inserted into the most dependent portion of the stomach and brought out on to the anterior abdominal wall (*Fig.* 2). Animals were allowed a 2-week recovery period before being used for experiments.

Pigs were deprived of food but not water for 24 hours before each study. No animal was used more than twice per week and never on successive days. The pigs were supported in modified Pavlov frames during the studies, each of which lasted 6 hours. After a 30-minute basal period Boots' secretin (1 u. $kg^{-1} h^{-1}$) and cholecystokinin (1 u. $kg^{-1} h^{-1}$) suspended in 0·15 M-NaCl were infused into an ear vein at 6 ml/h using a Braun Unita 1 infusion pump (B. Braun, Melsungen, West Germany) for the remainder of the study. The dose of secretin was that found to give half-maximal pancreatic volume and bicarbonate response (K_m dose), while that of cholecystokinin was twice that producing half-maximal protein response (twice K_m dose), on a background of secretin (1 u. $kg^{-1} h^{-1}$) in preliminary studies in the pig (Wheatley, 1975). This dose of cholecystokinin provided submaximal stimulation enabling changes in pancreatic protein secretion, particularly inhibition, to be observed during the study with alcohol. Within a further 90 minutes a stable pancreatic response was observed.

One of the following treatments was then superimposed on the background hormonal stimulation.

Intravenous alcohol

Absolute alcohol (96 per cent w/v, 0·5 ml/kg) was given by constant infusion into a jugular vein catheter for 2 hours and an infusion of 0·15 M-NaCl was given into a catheter in another jugular vein. Six studies were performed in 4 pigs leaving the gastric fistula open, and 8 studies in 3 pigs with the gastric fistula closed. Control studies were performed on 4 pigs using 0·15 M-NaCl 5 instead of alcohol. Five studies were performed with the gastric fistula open, and 5 with it closed.

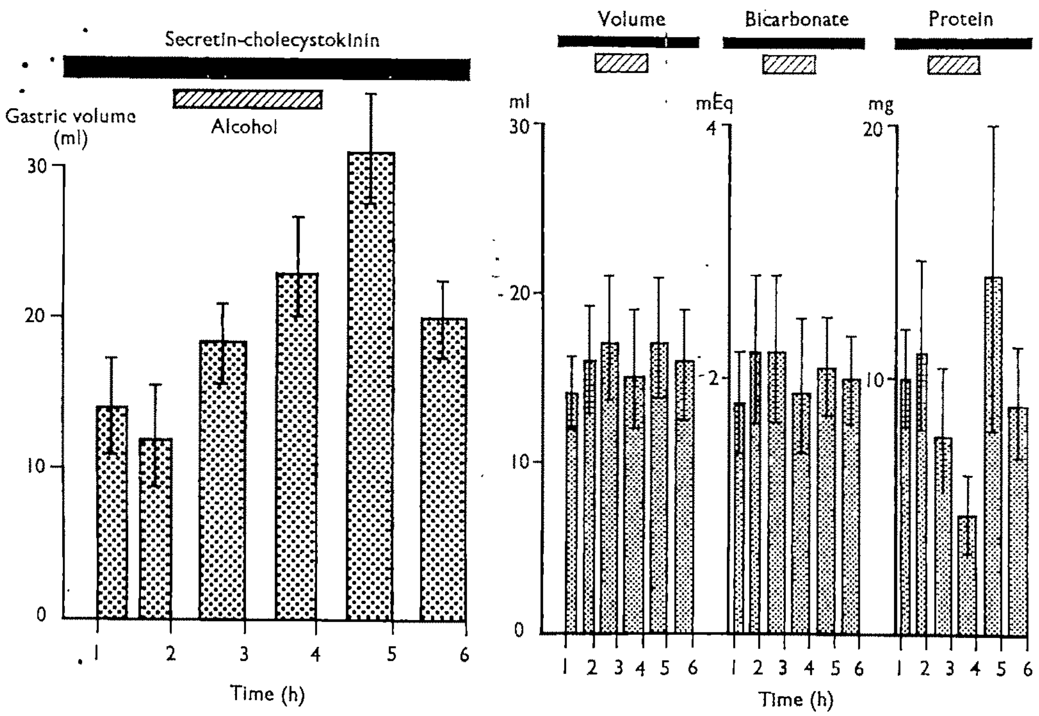
Intragastric alcohol

Five per cent alcohol (96 per cent w/v diluted in 0·15 M-NaCl) was infused into the stomach via the gastric cannula at the rate of 20 ml $kg^{-1} h^{-1}$ for 1 hour. The total dose of alcohol was the same as that given intravenously but it was given over 1 hour. Six studies were performed on 2 pigs. As a control study 15 per cent mannitol solution in 0·15 M-NaCl (approximately 1300 mosoml/l) was substituted for the 5 per cent alcohol. Four studies were performed on 2 pigs.

In both groups of experiments samples were collected every 15 minutes from the pancreatic and, where applicable, gastric cannulas. Pancreatic samples were measured for volume and stored on ice for estimation of bicarbonate and protein later in the day. Bicarbonate was estimated by adding 1 ml 0·1 M-HCl to 0·5 ml pancreatic juice, boiling and back-titrating to pH 7 with 0·1 M-NaOH using an automatic titrator (Radiometer, Copenhagen). Enzyme concentration was measured as total protein using the absorbance of an appropriately diluted sample at 280 nm on a Beckman spectrophotometer and comparing it with a standard bovine albumin solution. It has been shown that there is good correlation between the protein concentration of pancreatic juice and pancreatic enzyme (Keller et al., 1958). Gastric juice was measured for volume only as the degree of biliary reflux made acid estimation unreliable. Blood was taken for blood alcohol determinations at 30, 60, 120, 180 and 240 minutes after starting the alcohol infusion. For these an 'Ethyl Alcohol Stat-Pack' supplied by Calbiochem was used. Statistical comparisons were made using Student's *t*-test for unpaired values.

Results

The cannulas functioned satisfactorily for 4–5 weeks from the onset of studies, but after this time most pigs developed a small bowel fistula around the cannula. At autopsy this leak was found to occur between the



a *b*

Fig. 3. Changes in gastric and pancreatic secretion when intravenous alcohol was given with the gastric cannula open. *a*, Gastric volume; *b*, pancreatic juice volume, bicarbonate and protein output. Values expressed as the mean ±s.e.m./15 min.

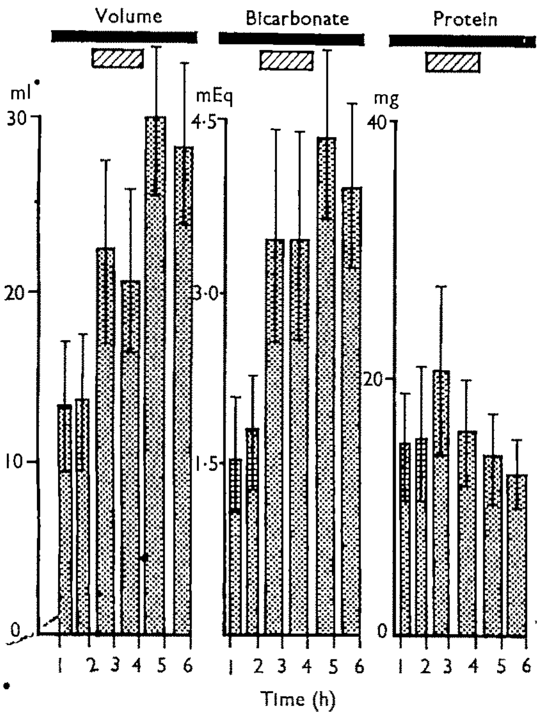


Fig. 4. Change in pancreatic secretion with intravenous alcohol and the gastric cannula closed. In all the studies secretin and cholecystokinin were infused after a 30-minute preliminary period.

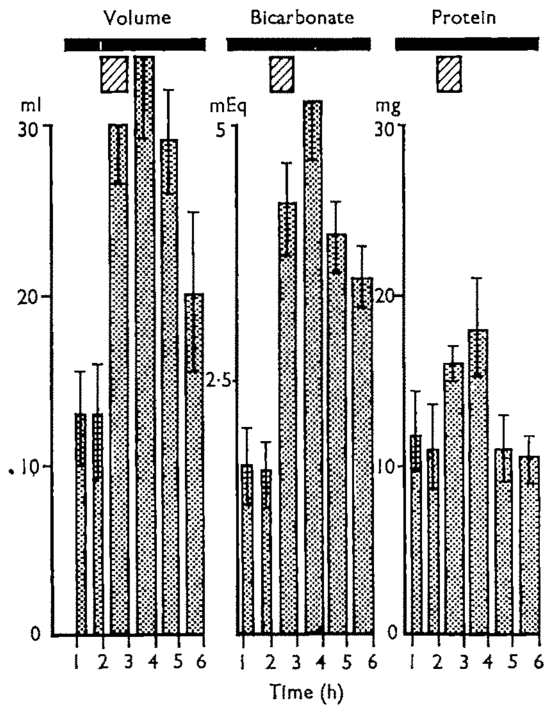


Fig. 5. Change in pancreatic secretion with intragastric alcohol.

cannula and the duodenal wall. The pancreas was histologically normal.

Intravenous alcohol

Intravenous alcohol produced the following effects. With the gastric cannula open the mean volume of gastric juice increased as alcohol was infused from 11 ± 2·5 ml to a peak of 31 ± 5·8 ml/15 min at 5 hours ($P < 0·05$) (*Fig.* 3*a*).

Owing to diversion of gastric acid away from the duodenum via the gastric cannula, there was no stimulation to pancreatic volume and bicarbonate secretion which did not vary significantly from basal (*Fig.* 3*b*). However, there was a significant depression in protein output from 11·4 ± 4·0 to 5 ± 1·5 mg/15 min ($P < 0·05$) at the end of the fourth hour of the study. This maximal depression coincided with the peak blood alcohol level which reached 0·09 mg/100 ml of blood.

In contrast, control studies with intravenous saline failed to show a depression in pancreatic protein secretion, which rose slightly from a basal level of 7·4 ± 3·2 to 10·3 ± 5·4 mg/15 min at the end of the fourth hour. This was not statistically significant.

Pancreatic secretion did not vary significantly from a mean basal volume of 6·5 ± 1·5 ml/15 min and bicarbonate secretion of 0·7 ± 0·21 mEq/15 min when saline was infused. With the gastric cannula closed (*Fig.* 4), allowing juice to enter the duodenum, intravenous alcohol caused a marked rise in mean pancreatic volume from 13·9 ± 5·0 to 30·6 ± 5·2 ml/15 min ($P < 0·05$) and in bicarbonate output from 1·6 ± 0·7 to 4·4 ± 0·9 mEq/15 min ($P < 0·01$). The peak rise was in the hour following the peak blood alcohol level. Protein output showed a rise at the start of the alcohol infusion from 15·8 ± 5·1 to 21 ± 6 mg/15 min, then fell gradually until the end of the study, but at no time was there a significant variation from basal.

Control studies with intravenous saline and a closed gastric cannula showed a slight rise in pancreatic secretion with time as basal gastric acid secretion presumably passed into the duodenum to release secretin. Pancreatic volume rose from 7·4 ± 2·7 ml to 10 ± 3 ml/15 min at the end of the study, while bicarbonate output rose from 0·85 ± 0·4 to 1·3 ± 0·5 mEq/15 min; neither increase was statistically significant. Protein also rose from 8·9 ± 3 mg to reach a peak of 11·4 ± 3 mg/15 min at the end of the fifth hour.

Intragastric alcohol

With intragastric alcohol given over 1 hour (*Fig.* 5) there was a pronounced and persistent rise in mean pancreatic volume from 12·6 ± 3·5 to 34·2 ± 5·0 ml/15 min ($P < 0·01$); bicarbonate output rose from 1·6 ± 0·5 to 5·2 ± 0·6 mEq/15 min ($P < 0·05$). In marked contrast to the study with intravenous alcohol and an open gastric cannula, there was a rise in protein output from 10·8 ± 2·2 to 17·7 ± 3·0 mg/15 min ($P < 0·05$).

It was noted that peak secretion was reached simultaneously with peak blood alcohol level 2 hours after starting the alcohol infusion via the gastric cannula (0·09 mg alcohol/100 ml blood).

Intragastric mannitol

Intragastric mannitol produced a rapid rise in pancreatic volume from 12·7 ± 1·7 to 29 ± 1·6 ml/15 min ($P < 0·05$) at the end of the third hour of the study, but then fell quickly towards the basal level so that at the end of the fourth hour it was down to 19·5 ± 4 ml/15 min, and at the fifth and sixth hours was 17 ± 4·5 and 14 ± 3 ml/15 min respectively.

This early peak and rapid fall contrasted with the change produced by intragastric alcohol where a peak at the fourth hour of 34·2 ± 5·0 ml/15 min was significantly higher than the level produced by mannitol of 19·5 ± 4 ml/15 min ($P < 0·05$) and persisted longer (*Fig.* 4). A parallel effect occurred with bicarbonate, which rose from 1·47 ± 0·3 to 4·1 ± 0·3 mEq/15 min ($P < 0·05$), then fell to 2·6 ± 0·5, 2·4 ± 0·6 and 1·8 ± 0·6 in successive hours, compared with the more pronounced and persistent rise seen with intragastric alcohol. The effect was repeated with protein, which rose from 11·4 ± 2·5 to 24·5 ± 7·5 mg/15 min, then fell to 19·4 ± 4·9, 14·9 ± 6 and 12 ± 4·5 mg/15 min in subsequent hours.

Discussion

In previous work on the effect of intravenous alcohol in the pig which was performed in antrectomized animals an increase in pancreatic volume and amylase output was noted (Hong and Magee, 1970). The authors concluded that the role of ethyl alcohol as a pancreatic stimulant was not clear. The present study is a composite investigation of the effects of intravenous and intragastric alcohol in a standard physiological pig model in one laboratory. The pig has not been commonly used for pancreatic studies, but has proved to be satisfactory for short term physiological studies. An attempt is being made to develop a long term pig model although rapid growth of the animals may render them unmanageable. The cannula will also require modification, perhaps by use of a flexible cross-connection to minimize leaks.

Alcohol has been shown to have two stimulatory effects on gastric acid secretion. Ingested alcohol stimulates the release of gastrin from the antrum, causing increased acid secretion (Woodward et al., 1957). Alcohol is also rapidly absorbed and then exerts its second systemic action, producing a further increase in gastric acid. This appears to be independent of the gastrin-releasing mechanism of intragastric alcohol and is blocked by anticholinergics (Hirschowitz et al., 1956). In this study a marked stimulatory effect of intravenous alcohol on gastric volume output was confirmed.

The increased acid produced by these two mechanisms passes to the duodenum where it causes the release of secretin (Bayliss and Starling, 1902; Epstein and Williams, 1961; Valenzuela et al., 1969), which in turn stimulates the pancreas to secrete bicarbonate and water. This is the main indirect or gastric-mediated response to alcohol. The present study has confirmed that this secretin-like effect is not a direct effect of alcohol on the pancreas, as the intravenous administration of alcohol with the gastric fistula open did not increase secretion of bicarbonate and water. On the other hand, when the gastric fistula was closed and acid allowed to enter the duodenum a typical pancreatic secretin-like response was observed.

The second effect of alcohol on the pancreas is direct. Gastrin is a weak stimulant of pancreatic enzyme secretion in the dog (Stening and Grossman, 1969) and possibly in man (Wormsley et al., 1966; Petersen and Berstad, 1973). The pancreatic protein response produced by intragastric alcohol would suggest that alcohol released gastrin in the pig and that this in turn acted on the pancreatic acini. The early rise in secretion noted after the administration of intragastric mannitol suggests that this effect may be partially osmotic. Release of cholecystokinin in the small bowel is also a possibility.

A third effect of alcohol on the pancreas is direct depression of enzyme secretion (Tiscornia et al., 1973; Solomon et al., 1974). This was confirmed in the present study where intravenous alcohol depressed pancreatic protein secretion when the gastric fistula was left open. The failure of intravenous alcohol to depress protein secretion in the experiments with the gastric cannula closed may be due to endogenous secretin potentiating the effect of the background infusion of a submaximal dose of cholecystokinin on pancreatic enzyme secretion, as potentiation between these two hormones is known to occur (Wormsley, 1969). There was no evidence of a diminished volume secretion by the pancreas, and no support was found for alcohol producing obstruction to pancreatic flow (Lowenfels et al., 1968). Of the gut hormones, glucagon is known to depress pancreatic protein output (Dyck et al., 1970). In other studies in our laboratory, intravenous glucagon has been shown to depress pancreatic enzyme secretion in secretin-stimulated pigs and in secretin + cholecystokinin-stimulated humans (Waterworth, Barbezat and Terblanche, 1973). One explanation for the depressed secretion noted with intravenous alcohol with the gastric cannula open may be a glucagon-mediated inhibition, as shown in *Fig.* 6. This will require further investigation. The response of the autonomic nervous system also warrants further examination in view of recent studies of the effect of vagotomy on pancreatic secretion (Konturek et al., 1974).

The exact role of alcohol in the pathogenesis of acute pancreatitis remains a mystery. Recent work has shown that dogs lose their ability to depress pancreatic secretion with alcohol when they are chronically fed on alcohol (Sarles et al., 1973). This was particularly evident with regard to protein secretion, and it was suggested that this protein, in relative excess, could form plugs in the pancreas. Calcium was low in the juice after alcohol ingestion, but this could be a result of precipitation in the protein plugs.

Other studies have shown a decreased incorporation of ^{32}P into phospholipids by the rat pancreas after alcohol ingestion; if the alcohol intake was prolonged the pancreas failed to recover normal function (Orreggo Matte et al., 1969). Similarly, ultrastructural damage to pancreatic tissue has been demonstrated after chronic alcohol ingestion (Darle et al., 1970). These changes are not unlike those seen with alcoholic damage to the liver, suggesting a direct toxic effect.

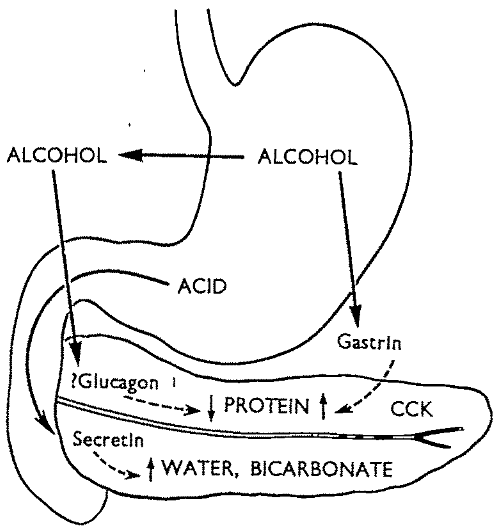


Fig. 6. Postulated mechanism for the actions of alcohol on pancreatic secretion.

Further understanding of the pathophysiology of alcohol and pancreatic function may provide the answer to alcohol-induced pancreatitis.

Acknowledgements

The advice and encouragement of Professor J. H. Louw are gratefully acknowledged. The studies were performed with the help of the staff of the J. S. Marais Surgical Laboratory, and Mesdames J. Fourie, J. Green, C. Rose-Innes and M. van Heerden performed the biochemical estimations.

Financial assistance was received from the Cape Provincial Administration, the Medical Research Council of South Africa and the Herman and Caporn Bequests to the University of Cape Town.

Mr D. Stewart of the Biomedical Engineering Department of Groote Schuur Hospital made the cannulas.

References

BAYER M., RUDICK J., LIEBER C. S. and JANOWITZ H. D. (1972) Inhibitory effect of ethanol on canine exocrine pancreatic secretion. *Gastroenterology* **63**, 619–626.

BAYLISS W. M. and STARLING E. H. (1902) The mechanism of pancreatic secretion. *J. Physiol.* (*Lond.*) **28**, 325–353.

DARLE N., EKHOLM R. and EDLUND Y. (1970) Ultrastructure of the rat exocrine pancreas after long-term intake of ethanol. *Gastroenterology* **58**, 62–72.

DAVIS A. E. and PIROLA R. C. (1966) The effects of ethyl alcohol on pancreatic exocrine function. *Med. J. Aust.* **2**, 757–760.

DREILING D. A., RICHMAN A. and FRADKIN N. F. (1952) The role of alcohol in the aetiology of pancreatitis. *Gastroenterology* **20**, 636–646.

DYKE W. P., TEXTER E. C., LASATER J. M. and HIGHTOWER N. C. (1970) Influence of glucagon on pancreatic exocrine secretion in man. *Gastroenterology* **58**, 532–539.

EPSTEIN A. M. and WILLIAMS R. D. (1961) Pancreatic response to alcohol following antral oesophagostomy. *Surg. Forum* **12**, 378–379.

HIRSCHOWITZ B. I., POLLARD H. M. and HARTWELL S. W. (1956) The action of ethyl alcohol on gastric acid secretion. *Gastroenterology* **30**, 244–256.

HONG S. S. and MAGEE D. F. (1970) Pharmacological studies on the regulation of pancreatic secretion in pigs. *Ann. Surg.* **172**, 41–48.

JANOWITZ H. D. and BAYER M. (1971) Alcohol and pancreatitis. *Ann. Intern. Med.* **74**, 444–445.

KELLER P. J., COHEN E. and NEURATH H. (1958) The proteins of bovine pancreatic juice. *J. Biol. Chem.* **233**, 344–349.

KONTUREK S. J., BECKER H. D. and THOMPSON J. C. (1974) Effect of vagotomy on hormones stimulating pancreatic secretion. *Arch Surg.* **108**, 704–711.

LOWENFELS A. B., MASCH B., LEE T. C. Y. and ROHMAN M. (1968) Effect of intravenous alcohol on the pancreas. *Arch. Surg.* **98**, 440–441.

MARKS I. N., BANK S. and LOUW J. H. (1974) Chronic pancreatitis in the Western Cape. *Digestion* **9**, 447–453.

MOTT C., SARLES H., TISCORNIA O. and GULLO L. (1972) Inhibitory action of alcohol on human exocrine pancreatic secretion. *Am. J. Dig. Dis.* **17**, 902–910.

ORREGGO MATTE H., NOVIA E., FERES A. and COSTA MAILLERE L. (1969) Ethanol ingestion and incorporation of ^{32}P into phospholipids of pancreas in the rat. *Gastroenterology* **56**, 280–285.

PETERSEN H. and BERSTAD A. (1971) Effect of pentagastrin on pancreatic secretion in man. *Scand. J. Gastroenterol.* **6**, 483–485.

PETERSEN H. and BERSTAD A. (1973) The interaction between pentagastrin and cholecystokinin on pancreatic secretion. *Scand. J. Gastroenterol.* **8**, 257–263.

SARLES H., TISCORNIA O., PALASCIANO G., BRASCA A., HAGE G., DEVAUX M. A. and GULLO L. (1973) Effects of chronic intragastric ethanol administration on canine exocrine pancreatic secretion. *Scand. J. Gastroenterol.* **8**, 85–96.

SOLOMON N., SOLOMON T. E., JACOBSON E. D. and SHANBOUR L. L. (1974) Direct effects of alcohol on *in vivo* and *in vitro* exocrine pancreatic secretion and metabolism. *Am. J. Dig. Dis.* **19**, 253–260.

STENING G. F. and GROSSMAN M. I. (1969) Gastrin related peptides as stimulants of pancreatic and gastric secretion. *Am. J. Physiol.* **217**, 262–266.

TISCORNIA O., GULLO L. and SARLES H. (1973) Inhibition of canine exocrine pancreatic secretion by intravenous ethanol. *Digestion* **9**, 231–240.

VALENZUELA J. E., UGARTE G. and PETERMANN M. (1969) Effects of intravenous ethanol on pancreatic secretion. *Gastroenterology* **56**, 1203.

WALTON B., SCHAPIRO H. and WOODWARD E. R. (1960) The effect of alcohol on pancreatic secretion. *Surg. Forum* **11**, 365–367.

WATERWORTH M. W., BANK S. and TERBLANCHE J. (1973) The development of a model of experimental pancreatitis in the pig. *S. Afr. J. Surg.* **11**, 110–111.

WATERWORTH M. W., BARBEZAT G. O. and TERBLANCHE J. (1973) The effect of glucagon on the pancreatic exocrine secretion in the human and the pig. *S. Afr. J. Surg.* **11**, 111.

WHEATLEY I. C. (1975) Unpublished observations.

WHEATLEY I. C., TERBLANCHE J., HICKMAN R. and BARBEZAT C. O. (1974) The effect of acute alcohol administration on exocrine pancreatic secretion in the pig. *Proc. Surg. Res. Soc. S. Afr. Durban.*

WOODWARD E. R., ROBERTSON C., RUTTENBERG C. and SCHAPIRO H. (1957) Alcohol as a gastric stimulant. *Gastroenterology* **32**, 727–737.

WORMSLEY G. (1969) A comparison of the response to secretin, pancreozymin and a combination of these hormones in man. *Scand. J. Gastroenterol.* **4**, 413–417.

WORMSLEY K. G., MAHONEY M. P. and NG M. (1966) Effects of a gastrin like penta peptide (I.C.I. 50, 123) on stomach and pancreas. *Lancet* **1**, 993–996.

Br. J. Surg. Vol. 62 (1975) 713–715

The effect of heparin and of acid-citrate-dextrose solution on screen filtration pressure of blood in experimental hypotension

B. J. PARDY AND H. A. F. DUDLEY*

SUMMARY

Anticoagulation with heparin may not always adequately protect an ischaemic vascular bed. A screen filtration device has been employed to study the in vitro actions of acid-citrate-dextrose (ACD) and heparin on blood from the dog in haemorrhagic shock. With both anticoagulants, blood obtained during shock caused greater filter obstruction than blood taken before shock. However, the increased obstruction was nearly four times greater with heparinized blood than with acid-citrate-dextrose blood. These findings suggest that the anticoagulant action of heparin may be markedly diminished in low blood flow states.

It is the standard practice of many surgeons to heparinize a regional vascular bed in which circulatory arrest is to occur on the premise that clotting will then be prevented. However, there is both clinical and experimental evidence that the use of heparin is not always successful: the lower limb sometimes does not recover after aortic cross-clamping, and although embolization may be blamed, clot is not always found; in rat kidney (Diethelm and Wilson, 1971) and adrenal (Kovács et al., 1966) and in rabbit brain (Ames et al., 1968) heparin has been ineffective in preventing microcirculatory obstruction.

Thus, it seemed important to establish if heparin effectively inhibited the tendency for fibrin to form under conditions of hypoperfusion. We have studied the changes in screen filtration pressure (SFP) of blood which occur with a standard shock preparation in the dog. The method is an indirect indication of any tendency of circulating blood to cause obstruction in the microcirculation, but is obviously influenced by many factors. For example, blood without anticoagulant and tested immediately causes little or no obstruction to a screen filter of 20 μ pore size (Swank, 1962); however, blood stored in acid-citrate-dextrose (ACD) for 3 weeks produces a marked obstruction, an effect thought to be the result of aggregation of platelets and leucocytes (Swank, 1961). The high SFP of ACD blood takes more than 2 days to develop, by comparison with 16–24 hours in heparinized blood (Swank, 1961). In that platelet aggregation can be induced easily in citrated plasma (Dhall et al., 1969), these observations suggest that the early rise in SFP in heparinized blood is likely to be caused by the development of fibrin. For a variety of reasons heparin is a relatively weak inhibitor of fibrin formation; indeed, heparinized blood cannot be stored for any length of time because of its tendency to produce fibrin clots (Mollison, 1972a). Finally, in relation to normal blood, red cell aggregation is unlikely to be important as a cause of screen filter obstruction (Dhall et al., 1969).

Variable results have been found for SFP in experimental exsanguination. On the one hand, blood without anticoagulant is said to cause marked filter obstruction, possibly because of an increased tendency of platelets and white cells to adhere rather than on account of the presence of preformed aggregates (Swank, 1962); on the other hand, a change in SFP has not been found in some breeds of dog (Swank et al., 1974). In the light of the effect of ACD and of heparin on normal blood, and of preliminary studies which had suggested increased SFP in blood from the dog in shock, a comparison was made between the two anticoagulants.

Materials and methods

The screen filtration technique was essentially that of Swank (1961). The 20 μ filter was mounted in a stainless steel block heated to 37 °C; blood or saline was forced through the system with a mechanical ram attached to a plastic syringe. Pressure was transduced from a side-arm with a strain gauge and traced on a chart recorder. A 2-ml syringe driven at a flow rate of 1 ml/7 sec and a 5-ml syringe at 1 ml/3·8 sec were used for blood and saline respectively. The filter was calibrated with 2 ml of saline; 0·7 ml of blood (5 sec filtration) was then passed through, followed by a further 2 ml of saline. The difference between the two saline pressures gives an indication of the degree of obstruction produced by the blood.

Preparation of heparinized and ACD blood was standardized. A heparin concentration of 3 i.u./ml is required to prevent normal human blood from clotting *in vitro* (Mollison, 1972b), and preliminary studies confirmed that this level would prevent change in SFP for up to 1 hour at 37 °C. Consequently, and because of the expected greater coagulability of the blood of the experimental animal, a level of 5 i.u./ml was decided upon. Heparin Injection (mucous) BP without bacteriostatic (Paines & Byrne Ltd) containing 1000 i.u./ml was diluted 1 : 30 with normal saline; 110 μl were then inserted into a siliconized 2-ml syringe (Silicone Fluid MS 1107, Hopkins & Williams Ltd). A similar quantity of ACD (NIH Solution A) (Mollison, 1972c) was placed in a further 2-ml syringe. Blood obtained by needle puncture of the femoral vein into a siliconized 5-ml syringe was

---

* Surgical Unit, St Mary's Hospital, London.

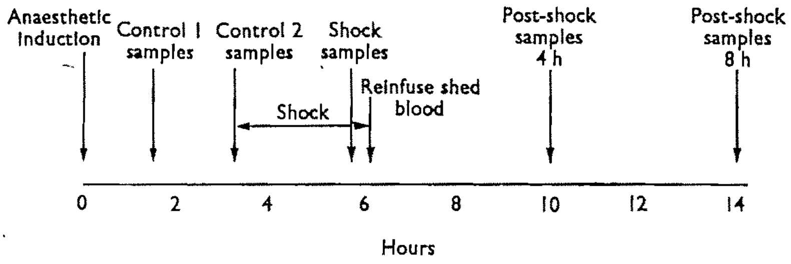


Fig. 1. Plan of the experiment.

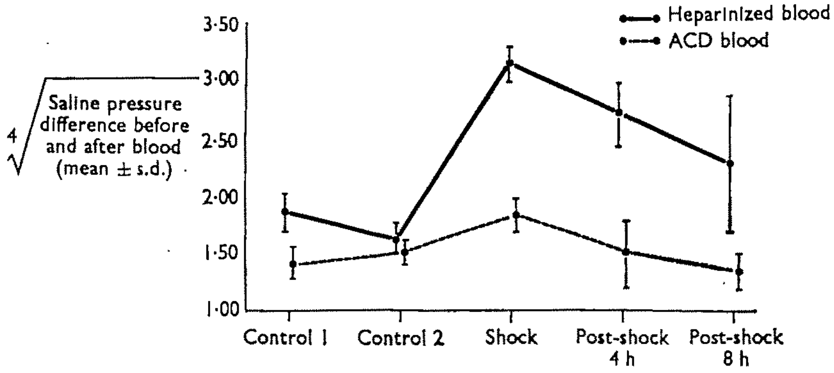


Fig. 2. Effect of haemorrhagic shock on screen filter obstruction by heparinized and ACD blood.

Table I. CHANGES IN ARTERIAL PRESSURE AND MIXED VENOUS Po_2 AND pH

	Control 1	Control 2	Shock	Post-shock 4 h	Post-shock 8 h
Arterial pressure (mm Hg)	201 ±9·7	202 ±11·8	88 ±10·2	184 ±21·9	186 ±20·2
Pvo_2 (mm Hg)	51 ±3·0	48 ±2·1	24 ±4·6	44 ±1·5	43 ±2·1
pHv	7·406 ±0·011	7·402 ±0·020	7·168 ±0·051	7·362 ±0·033	7·390 ±0·016

Results given as mean ±s.d.

aspirated into the prepared syringes in such a quantity as to give a final heparin concentration of 5 i.u./ml in blood at a PCV of 45 per cent. The plasma ACD concentration was approximately that of ACD in whole blood also at a PCV of 45 per cent, that is 1 : 9. The two samples were placed on a mixing table for 1 minute and then in a waterbath at 37 °C. After 1 hour SFP was measured. Coincidentally, a mixed venous blood sample for hydrogen ion activity (pH) and oxygen tension (Pvo_2) was withdrawn from a pulmonary artery catheter and measured with a micro-electrode system. Shock was induced in 5 greyhounds of mean weight 27 kg. The procedure is summarized in *Fig.* 1.

Filter resistance was expressed as the fourth root of the measured pressure. Statistical analysis was by the Walsh test for non-parametric paired data (Siegel, 1956).

Results

Changes in mean arterial pressure and mixed venous Po_2 and pH are seen in *Table I*. The comparison between blood treated with ACD and with heparin is shown in *Fig.* 2. At all stages heparinized blood caused greater obstruction than did ACD blood. The pooled values in the control periods differ significantly from each other ($P = 0·005$). During shock SFP is increased; 0·38 ± 0·14 (mean ± s.d.) for ACD blood, and 1·49 ± 0·60 for heparinized blood. The incremental ratio is 1 : 3·9, that is, heparin is nearly four times less effective than ACD in the prevention of increased filter obstruction by blood from the dog during shock.

Discussion

These results show that change in SFP during and after haemorrhagic hypotension in the dog is dependent upon the anticoagulant used. Heparin is associated with a marked increase. Although the evidence is, as already discussed, indirect, it is probable that the obstruction is the result of fibrin formation.

There are a number of factors which might cause this ineffectivity of heparin. Increased thromboplastin activity nullifies its anticoagulant action (Jaques, 1963); platelet consumption with thromboplastin release is a known accompaniment of hypovolaemic hypotension. Paracoagulation of soluble fibrin monomer complex by lysosomal protein fraction of polymorphonuclear leucocytes may also be of significance because heparin at the concentration used does not prevent this form of precipitation of fibrin (Hawiger et al., 1969). Further, lysosomal enzymes are released during haemorrhagic shock (Clermont et al., 1972) and these directly antagonize heparin (Stamm, 1966). Mild acidity interferes with the anticoagulant activity of heparin (Jensen et al., 1948; Crowell and Houston, 1961; Hardaway et al., 1964), but in the current study high SFPs were present at normal pH. Finally, heparin consumption or degradation may interfere with its anticoagulant properties in the animal in shock. Whatever the cause of the increased SFP of heparinized blood in the preparation studied, the evidence is presumptive that a microcirculatory problem might still persist despite the use of heparin. The same may well be true for a regional circulation in which the flow of blood is arrested. A reassessment of heparin for both general and regional use seems called for.

Acknowledgement

We are grateful for a grant from the Wellcome Trust which helped support this work.

References

AMES A., WRIGHT R. L., KOWADA M., THURSTON J. M. and MAJNO G. (1968) Cerebral ischaemia II, the no-flow phenomenon. *Am. J. Pathol.* **52**, 437–454.

CLERMONT G. H., ADAMS J. T. and WILLIAMS J. S. (1972) Source of lysosomal enzymes acid phosphatase, in haemorrhagic shock. *Ann. Surg.* **175**, 19–25.

CROWELL J. W. and HOUSTON B. (1961) Effect of acidity on blood coagulation. *Am. J. Physiol.* **201**, 379–382.

DHALL D. P., ENGESET J., MCKENZIE F. N. and MATHESON N. A. (1969) Screen filtration pressure of blood—an evaluation. *Cardiovasc. Res.* **3**, 147–154.

DIETHELM A. G. and WILSON S. J. (1971) Obstruction to the renal microcirculation after temporary ischaemia. *J. Surg. Res.* **11**, 265–276.

HARDAWAY R. M., ELOVITZ M. J., BREWSTER W. R. and HOUCHIN D. N. (1964) Clotting time of heparinised blood. *Arch. Surg.* **89**, 701–705.

HAWIGER J., COLLINS R. D. and HORN R. G. (1969) Precipitation of soluble fibrin monomer complexes by lysosomal protein fraction of polymorphonuclear leukocytes. *Proc. Soc. Exp. Biol. Med.* **131**, 349–353.

JAQUES L. B. (1963) The chemistry, pharmacology and assay of heparin. *Thromb. Diath. Haemorrh.* **11**, (Suppl.) 27–36.

JENSEN R., SNELLMAN O. and SYLVÉN B. (1948) On the inhomogeneity of commercial heparin preparations from the physicochemical point of view. *J. Biol. Chem.* **174**, 265–271.

KOVÁCS K., CARROLL R. and TAPP E. (1966) Temporary ischaemia of the rat adrenal gland. *J. Pathol.* **91**, 235–240.

MOLLISON P. L. (1972a) *Blood Transfusion in Clinical Medicine*, 5th ed. London, Blackwell, p. 57.

MOLLISON P. L. (1972b) *Blood Transfusion in Clinical Medicine*, 5th ed. London, Blackwell, p. 10.

MOLLISON P. L. (1972c) *Blood Transfusion in Clinical Medicine*, 5th ed. London, Blackwell, p. 686.

SIEGEL S. (1956) *Nonparametric Statistics for the Behavioral Sciences.* New York, McGraw-Hill, pp. 83–87.

STAMM H. (1966) Antiheparine. *Thromb. Diath. Haemorrh.* **19** (Suppl.), 181–186.

SWANK R. L. (1961) Alteration of blood on storage: measurement of adhesiveness of 'aging' platelets and leukocytes and their removal by filtration. *New Engl. J. Med.* **265**, 728–733.

SWANK R. L. (1962) Adhesiveness of platelets and leukocytes during acute exsanguination. *Am. J. Physiol.* **202**, 261–264.

SWANK R. L., CONNELL R. S. and WEBB M. C. (1974) Dacron wool filtration and hypotensive shock: an electron microscopical study. *Ann. Surg.* **179**, 427–433.

Br. J. Surg. Vol. 62 (1975) 716–719

Acute segmental ischaemic enteritis in Thailand

THEODORE P. WELCH AND SOMSAK SUMITSWAN*

SUMMARY

A disease characterized by segments of ischaemic small intestine has been recognized in northern Thailand over the past decade. The clinical features and appearance of the diseased intestine are described. Most of the patients were treated by surgical resection of the affected bowel. The overall mortality was 14 per cent. Recently, some patients have been successfully treated by non-surgical means. The aetiology of the disease is still unknown.

THE first 5 cases of acute segmental ischaemic enteritis recognized at the Chiang Mai University Hospital were described by Headington et al. in 1967. Since that time this disease has been encountered in several more patients. This paper describes 50 cases seen between 1962 and 1972. The following case history illustrates the typical clinical picture.

Case report

A 5-year-old Thai boy was admitted on 21 April 1970 with a 4-day history of generalized abdominal pain accompanied by fever for 3 days. The day before admission he had developed diarrhoea with frank blood. On admission his pulse was 160/min and he was clinically dehydrated. He had a distended, silent abdomen. There was no localized tenderness. Rectal examination was normal apart from the fact that he had liquid, bloody diarrhoea.

Investigations revealed the following: haemoglobin 13·3 g per cent, haematocrit 42, white cell count 8300/mm^3, CO_2 reserve 4 mEq/l. An abdominal X-ray showed dilated small bowel and thickened bowel wall of the lower jejunum.

The patient's dehydration and acidosis were corrected preoperatively. At laparotomy it was found that apart from the first 90 cm of jejunum all the jejunum and ileum showed ischaemic changes. The bowel wall was a deep red colour and showed no evidence of peristalsis. It was felt that the patient could not survive if all the affected intestine was resected, so the intestine was decompressed and the abdomen closed. The patient was treated with intravenous tetracycline (250 mg 6-hourly) and hydrocortisone (100 mg 6-hourly). He made a good recovery. His diarrhoea stopped after the operation and he was discharged on the twelfth postoperative day. He was seen for follow-up in September 1971 and appeared well. He was well nourished and had normal bowel function. His haemoglobin was 11·5 g per cent.

Patients and methods

The clinical records of 50 patients were analysed. The diagnosis of segmental ischaemic enteritis was made on clinical, radiological and histological grounds. The ages of the patients studied ranged from 1 year and 10 months to 60 years. Seventy per cent of the patients were males (*Table I*).

Symptoms and signs

The duration of symptoms preceding admission ranged from 1 to 10 days with an average of 2·9 days. The first symptom was usually generalized abdominal pain, which was soon followed by diarrhoea and fever. In 74 per cent of the cases the diarrhoea had frank blood, either from the outset of the diarrhoea or from soon afterwards. Nausea and vomiting were commonly present. The admission symptoms are tabulated in *Table II*. None of the patients gave a history of recent abdominal trauma or a period of hypotension preceding the onset of symptoms.

Table I: AGE AND SEX DISTRIBUTION

	Males		Females		Total	
Age group	No.	%	No.	%	No.	%
0–5	6	12	1	2	7	14
6–9	13	26	1	2	14	28
10–19	9	18	4	8	13	26
20–29	5	10	1	2	6	12
30–39	1	2	3	6	4	8
40+	1	2	5	10	6	12

Table II: SYMPTOMS AND SIGNS

Symptom or sign	No. of cases	%
Nausea and vomiting	37	74
Abdominal pain	34	68
Diarrhoea	41	82
Bloody diarrhoea	37	74
Pyrexia above 38 °C	24	48
Shock	7	14
Clinical dehydration	35	70
Abdominal tenderness	40	80
Loss of bowel sounds	25	50

Table III: LABORATORY FINDINGS

Investigation	No. of cases	%
Haemoglobin <10 g per cent	6	12
Leucocytosis		
10 000–20 000/mm^3	26	52
>20 000/mm^3	12	24
Blood in stool*	44	100

* In 44 patients examined.

On examination a low grade fever was common. Twenty-four (48 per cent) of the patients had a temperature above 38 °C on admission. The highest temperature recorded on admission was 40 °C. Tachycardia was common (43 patients), but shock was found in only 7 patients. Clinically, many of the patients appeared dehydrated. A mild degree of abdominal distension was seen in half the patients. Abdominal tenderness was common (80 per cent of cases), but there was seldom any marked guarding or rigidity. Ascites was not detectable clinically. The bowel sounds were usually decreased, and in 50 per cent of the patients there was an absence of bowel sounds (*Table II*).

---

* Department of Surgery, Faculty of Medicine, University of Chiang Mai, Thailand.

Laboratory investigations

Six patients had a haemoglobin of less than 10 g per cent (*Table III*). Twenty-six had a leucocytosis of between 10 000 and 20 000/mm^3 and 12 had a leucocytosis above 20 000/mm^3. The neutrophil count was usually about 80 per cent, with a shift to the left. Platelet counts and estimations of prothrombin time in 3 patients were normal.

The faeces of 88 per cent of the patients were examined and all were found to contain blood. Parasites were found in 10 of 27 specimens of faeces examined. The parasites were hookworm, tapeworms, *Ascaris*, strongyloid larvae and *Opisthorchis* ova. Cultures were performed on 6 patients' faeces. One produced a growth of *Clostridium perfringens*. The others grew only normal gut commensals (none of these was an anaerobic culture).

Radiography

In the cases presenting early, anteroposterior upright and supine X-rays of the abdomen showed evidence of paralytic ileus with dilated loops of small bowel. In cases with a longer history short loops of small bowel were dilated and there was often thickening of the wall of the affected segments and an appearance of fixation. The distance between contiguous loops was widened. There was often evidence of free fluid in the abdominal cavity (*Fig.* 1). No barium studies were done.

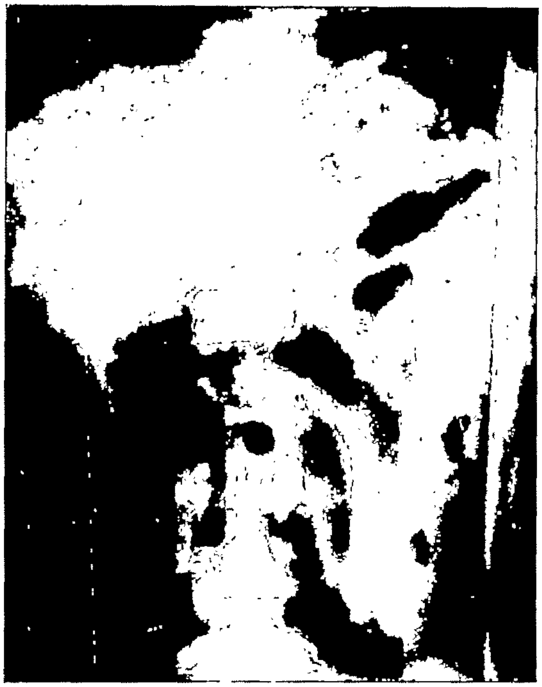


Fig. 1. X-ray showing dilated loops of small bowel and the presence of peritoneal fluid. There is thickening of the bowel wall.

Treatment and clinical course

All the patients in the series, except those who were diagnosed at autopsy as well as 6 others, underwent surgery. At laparotomy a length of small intestine showed ischaemic changes. In the early stages the bowel wall looked thickened and pale and there were often subserosal petechiae. In the later stages parts of the affected segment were deep red and friable. In 3 patients there were perforations of the affected bowel. In 29 patients (58 per cent) the segment was less than 100 cm long. The ischaemic segment was most commonly found in the jejunum (62 per cent). In 8 patients it was located in the ileum, and in 5 it affected both the jejunum and ileum. In 2 patients there appeared to be two affected segments separated by 15 cm of normal-looking intestine. In both these patients the lesions were in the lower jejunum and upper ileum. One patient was operated on for a perforated duodenal ulcer and the ischaemic segment of jejunum was found and resected. The duodenal ulcer was closed by simple suture. All the patients had enlarged mesenteric glands and free fluid, usually straw-coloured and odourless, in the peritoneal cavity. The mesenteric arteries were always found to be pulsatile and there was no evidence of arterial or venous thrombosis outside the bowel wall.

The patients not treated by surgical resection of the diseased intestine were all treated with tetracycline (250 mg 6-hourly) and hydrocortisone (100 mg 6-hourly) intravenously and intravenous fluids and nasogastric suction. They were allowed to take oral liquids and diet when the abdominal pain settled and they no longer had bloody diarrhoea.

Forty-three of the 50 patients survived. Of the 7 who died, 3 were diagnosed at autopsy. Another patient had prolonged postoperative diarrhoea and abdominal distension followed by dehiscence of the abdominal wound. A fifth had a gastrostomy done for dilatation of the stomach and this leaked, causing fatal complications. A sixth died from septicaemia and at autopsy was found to have miliary abscesses in the lungs. The remaining patient developed a faecal fistula and disrupted wound. The average duration of stay in hospital was 17 days.

It has been interesting to confirm Headington's observation (Headington et al., 1967) that the disease is most commonly seen during the rainy season (that is, between May and November). Only 3 patients were seen outside that time.

Pathological findings

In every case the ischaemic bowel was limited to the small intestine. No involvement of the duodenum, appendix or colon was seen. The area of transition between the normal bowel and the affected segment was not more than 3–4 cm wide and in most cases there was a distinct line of demarcation. The intestinal wall was thickened, producing relative narrowing of the lumen. The mucosa looked oedematous and haemorrhagic but no superficial ulceration was seen.

Microscopically, there was haemorrhagic necrosis and inflammatory oedema involving the mucous membrane, submucosa and muscularis mucosa. There was coagulative necrosis of the tips of the plicae. Thrombosis of the intramural vessels was commonly seen and in 2 cases an Arthus-like phenomenon was seen. The bowel wall was infiltrated with inflammatory cells—histiocytes, round cells and some polymorphonuclear leucocytes. The serosa contained a serous exudate with a few cells. Lymph glands showed hyperplasia with some haemorrhage into the glands, but no loss of nodal pattern. Gram stains failed to reveal a common pathogen. Associated parasites are described under laboratory investigations.

Discussion

Acute segmental ischaemic enteritis is an uncommon condition which mainly affects young people. It is characterized by an ischaemic length of small intestine. The ischaemic changes may be reversible. It is possible to make a confident preoperative diagnosis in most patients. The characteristic findings are abdominal pain associated with a mild fever and bloody diarrhoea.

In Pig-bel disease, which has been described in New Guinea (Murrell et al., 1966), lengths of ischaemic intestine have been found. A β-toxin-producing strain of *Clostridium perfringens* (*Clostridium welchii*) has been implicated (Egerton, 1966). The disease may be related to the ingestion of food which is infected or produces a localized allergic reaction. The vessels supplying the small intestine appear normal both macroscopically amd microscopically.

Acute segmental ischaemic enteritis as seen in Thailand has some features in common with Pig-bel disease. We feel that the disease in Thailand is a different disease from Pig-bel despite the fact that both are characterized by ischaemia and necrosis of lengths of small intestine. Both diseases are most commonly seen in children and young adults and are more frequent in males (Murrell, 1966). Pig-bel disease has often occurred in epidemics following pig feasts. The similar condition in Thailand has only been recognized in scattered, individual cases. The following features noted in Pig-bel disease have not been found in acute segmental ischaemic enteritis in Thailand: marked abdominal distension with a *very tender* abdomen, the presence of smelly, serosanguinous fluid in the peritoneal cavity, discoloured fibrinous exudate on the small bowel and an intensely haemorrhagic, swollen and oedematous mesentery (Roth, 1966). Residual multiple stenosis and short-circuited loops with resulting malnutrition and malabsorption have been described in Pig-bel disease. None of these features has been seen in any of the patients with acute segmental ischaemic enteritis.

The presence of parasites in the gastro-intestinal tract of patients affected by acute segmental ischaemic enteritis was not higher than the expected incidence in northern Thailand (Cunningham et al., 1970). There is no evidence to implicate parasites as an aetiological factor.

Acute segmental ischaemic enteritis closely resembles the condition described by Zeissler et al. (1949). They were able to identify a bacillus which they called '*Cl. welchii* type F' from specimens obtained from several patients with enteritis necroticans. They described colonies of this organism having smooth single rods with no flagella. Its spores showed high thermal resistance. The bacillus produced traces of *Cl. welchii* α-toxin and considerable quantities of β-toxin. Injections of a 1-day-old culture into guinea-pig intestine led to the development of enteritis necroticans, and they concluded that the damage to the intestine was due to the β-toxin of *Cl. welchii* type F. It is unfortunate that extensive bacteriological studies were not done on specimens obtained from our patients, for it seems very likely that the condition seen in Thailand and that described by Zeissler et al. are the same disease.

After Headington et al. (1967) diagnosed the first 2 cases of acute segmented ischaemic enteritis at autopsy, his next 3 patients were treated by resection of the affected segment of intestine and survived. In a patient whose case history is described above almost all the small intestine appeared ischaemic and no resection was performed. The abdomen was closed and postoperatively the patient made a good recovery. Six patients have since been successfully treated without resection of the ischaemic intestine. Another patient, a 24-year-old man, appeared to be doing well with steroids and broad spectrum antibiotic therapy. On the eighth day of treatment he was rather unwisely given a bowl of meat, vegetables and noodles, having previously only taken sips of water. Soon afterwards he developed severe abdominal pain and at laparotomy was found to have multiple perforations in a segment of ischaemic jejunum. Following resection of this length of jejunum he made a good recovery.

We feel that non-operative treatment is the treatment of choice for patients in the early stages of the disease. Six patients have now survived without resection of intestine. These patients were treated with broad spectrum antibiotics (usually tetracycline 250 mg 6-hourly intravenously) and hydrocortisone (100 mg 6-hourly intravenously). This treatment is empirical as the aetiology of the disease is unknown. Patients being treated in this way must be observed closely as they are liable to develop gangrene of the bowel wall and perhaps perforation. Conservative treatment may be best for patients in the early stages of the disease, but once gangrene is established and the viability of the bowel wall is seriously threatened, or if perforation occurs, surgery is necessary.

Although this disease is not common, it does offer a challenge for further investigation to discover its cause. Professor Black's suggestion (1966) that epidemiological and anthropological studies might shed light on the aetiology of Pig-bel disease might equally apply to acute segmental ischaemic enteritis.

Acknowledgement

We thank Dr B. D. Morson of St Mark's Hospital, London, for encouragement and advice in the preparation of this paper.

References

BLACK R. H. (1966) Pig-bel—summing up. *Papua New Guinea Med. J.* 9, 73.

CUNNINGHAM C. E., DOEGE T. C. and BANGXANG H. N. (1970) *Studies of Health Problems and Health Behaviour in Saraphi District, North Thailand.* Faculty of Medicine, Chiang Mai University, pp. 3–13.

EGERTON J. R. (1966) Bacteriology of enteritis necroticans in New Guinea highlanders. *Papua New Guinea Med. J.* **9**, 55–59.

HEADINGTON J. T., SATHORNSUMATHI S., SIMARK S. and SUJATANOND W. (1967) Segmental infarcts of the small intestine and mesenteric adenitis in Thai children. *Lancet* **1**, 802–806.

MURRELL T. G. C. (1966) Some epidemiological features of Pig-bel. *Papua New Guinea Med. J.* **9**, 39–50.

MURRELL T. G. C., ROTH L., EGERTON J., SAMELS J. and WALKER P. D. (1966) Pig-bel: enteritis necroticans. *Lancet* **1**, 217–222.

ROTH L. (1966) Diagnosis and management of Pig-bel. *Papua New Guinea Med. J.* **9**, 51–54.

ZEISSLER J. and RASSFELD-STERNBERG L. (1949) Enteritis necroticans due to *Clostridium welchii* type F. *Br. Med. J.* **1**, 267–269.

Br. J. Surg. Vol. 62 (1975) 720–726

Cause and management of high volume output salt-depleting ileostomy

G. L. HILL, W. S. J. MAIR AND J. C. GOLIGHER*

SUMMARY

Ileostomy function was studied in 12 patients with an established ileostomy following proctocolectomy, in 6 of whom minimal amounts (less than 9 cm) and in 6 significant amounts (30–120 cm, mean 60 cm) of terminal ileum had been removed.

Patients who had undergone significant ileal resection had daily faecal volumes considerably greater than those with minimal ileal resection (1202 ± 284 ml versus 401 ± 92 ml, $P < 0{\cdot}001$), and also greater daily outputs of sodium (146 ± 53 mEq versus 43 ± 12 mEq) and potassium (12·7 ± 9·0 mEq versus 4·0 ± 0·99 mEq). The percentage water content of the ileostomy fluid was greater in patients who had had the ileum resected (93·1 ± 1·8 per cent versus 89·8 ± 2·5 per cent). In addition, the sodium/potassium ratio in the urine in patients with a properly acting ileostomy after ileal resection was low.

It is concluded that when recurrent inflammatory bowel disease, partial small bowel obstruction and intraperitoneal sepsis have been excluded there remains a number of patients whose high ileostomy output is due entirely to the amount of ileum resected.

The management of patients with a high output ileostomy with codeine phosphate, Lomotil and oral administration of sodium chloride tablets is discussed.

THE majority of patients who have an ileostomy live an apparently normal life and appear unaffected by the chronic loss of water and sodium from their ileal fistula. However, the susceptibility of ileostomy patients to sodium depletion has been clearly demonstrated (Gallagher et al., 1962). Direct studies of body composition have shown deficits in both water and body salt (Clarke et al., 1967), and deficits occurring before surgery are not repaired once the ileostomy is established (Hill, Goligher et al., 1975). Particularly susceptible to water and salt depletion are patients in whom the ileostomy volume is abnormally large. After recurrent inflammatory bowel disease, partial intestinal obstruction and intraperitoneal sepsis have been excluded there remains a group of patients with a high volume salt-losing ileostomy in whom no particular cause for this complication can be found. This report describes the aetiology of the profuse ileostomy output in this type of patient and outlines how this problem may be managed.

Patients and methods

Twelve patients who had had an ileostomy for more than 6 months were studied. The clinical details of each patient are given in *Table I*, from which it will be seen that *Cases* 1–6 had had minimal ileal resection (4–9 cm), whilst *Cases* 7–12 had undergone significant excision of ileum (30–120 cm). At the time of the study all the patients were well and living active lives and none had had any alteration in ileostomy function over the preceding few months. There was no clinical evidence of recurrent disease or of ileostomy stenosis in any of the patients and none was taking any medication during the period of study.

All the patients were studied for 3 days in hospital. During this time they were on a normal diet apart from the fact that no additional salt was permitted with meals. Each 24 hours the total output of ileostomy and of urine was collected and recorded and the amounts of sodium and potassium in these fluids were determined. In the case of ileostomy fluid the electrolyte concentrations were measured on the supernatant of an aliquot of aqueous homogenate using an EEL Integrating Flame Photometer no. 227. The water content of the ileostomy fluid was determined by taking aliquots of known weight (A) and drying to constant weight (D). Then, from the total weight of the ileostomy fluid (F) and the weight (W) of distilled water added, the water content was calculated as follows:

$$\text{Water (per cent)} = 100\left(1 - \frac{D(F+W)}{FA}\right).$$

In addition, *Cases* 3, 10 and 11 were investigated in more detail over a 12-month period. Collections of ileostomy fluid and of urine were made on the first 11 postoperative days after the ileostomy was established. Similar collections were obtained at 1, 6 and 12 months after operation. At 12 months *Cases* 10 and 22 underwent a 12-day study in a metabolic ward. During the first 4 days of this period the patients were on a normal diet containing sufficient calories calculated to provide maintenance requirements appropriate to each patient's weight and activity. No additional salt was provided with the diet and care was taken to avoid prune juice, quantities of cooked cabbage, etc. —substances which are known to increase ileostomy output (Kramer et al., 1962). During the entire study period 24-hour collections of ileostomy fluid and of urine were made. At the end of the 4-day control period the patients were given codeine phosphate 45 mg by mouth every 6 hours for another 4 days. At the conclusion of the second 4-day collection period (on day 9), whilst continuing on the normal diet and codeine phosphate medication, oral sodium chloride was added in a dose of 2 g every 6 hours, and the codeine and salt were continued at these dosages until the end of the study on day 12. The results were statistically evaluated by calculating the mean values ± 1 s.d. and applying the non-paired *t*-test.

---

* University Department of Surgery, The General Infirmary, Leeds.

Findings

Volume of ileostomy output

Table I shows that *Cases* 1–6 had considerably smaller faecal volumes than *Cases* 7–12. The mean 24-hour faecal volume measured over the 3-day period was 401 ± 92 ml for *Cases* 1–6 (low volume group) compared with 1202 ± 284 ml ($P < 0{\cdot}001$) for *Cases* 7–12 (high volume group) (*Table II*). The mean age of the low volume group was 47·3 years (range 29–63 years) compared with 40·3 years (range 27–71 years) for the high volume group. The mean body weight of the low volume group was slightly less than that of the high volume group (56·8 ± 12·7 kg and 58·4 ± 10·0 kg respectively). Apart from a preponderance of males in the high volume group, the most striking attribute of these patients appears to be the fact that each had had an ileal resection (*Table I*).

Chemistry of ileal effluent

Table II compares the ileostomy chemistry in the low volume group with that of the high volume group. The water content in the low volume cases was significantly less than in the high volume cases. The concentration of sodium and potassium in the ileostomy fluid, however, was not significantly different between the two groups. The Na/K ratio in the ileostomy fluid was significantly lower in the low volume group. This difference was even more marked when *Case* 7 was excluded; he had a Na/K ratio in his ileostomy fluid of 2·8 and no sodium could be detected in his urine.

Changes in quantity and composition of ileostomy output on serial studies

Low volume output ileostomy: *Fig.* 1 illustrates the pattern of ileostomy function of *Case* 3, who was followed from the day his ileostomy was established for intervals up to 12 months. At no period was this patient on steroids. His ileostomy behaviour is typical

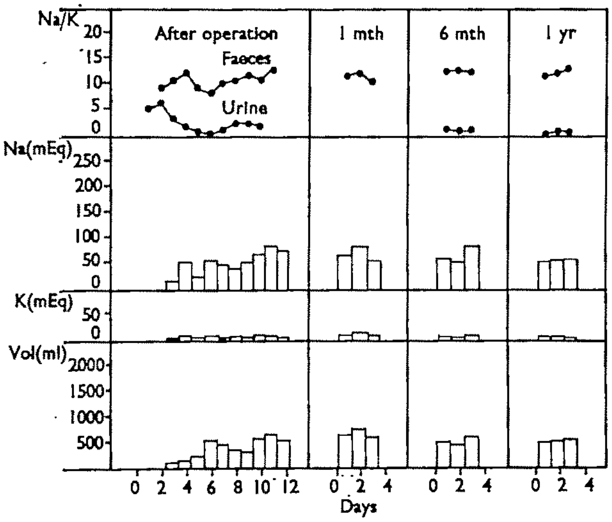


Fig. 1. Ileostomy chemistry in *Case* 3 measured at intervals over a 1-year period dating from the day of operation. Each vertical column in the histograms represents the output over a 24-hour period.

Table I: CLINICAL DATA OF 12 ILEOSTOMY PATIENTS

Case	Sex	Age (yr)	Weight (kg)	Final diagnosis	Ileal resection (cm)	24-Hour ileostomy volume (ml)
1	F	40	48·3	Ulcerative colitis	7·5	310±30
2	F	41	56·3	Ulcerative colitis	8·8	353±68
3	M	29	53·7	Ulcerative colitis	7·5	530±27
4	F	63	48·6	Ulcerative colitis	6·3	470±90
5	F	58	52·1	Granulomatous disease	8·8	387±38
6	M	53	82·0	Polyposis coli	3·8	356±76
7	M	56	57·1	Ulcerative colitis	37·5	1066±58
8	M	33	66·3	Granulomatous disease	120·0	843±171
9	M	38	54·9	Granulomatous disease	45·0	1343±323
10	M	31	59·2	Granulomatous disease	60·0	1543±95
11	M	27	63·3	Ulcerative colitis	68·0	1033±49
12	F	71	49·6	Granulomatous disease	30·0	1386±135

Table II: BIOCHEMICAL FINDINGS IN ILEOSTOMY FLUID ACCORDING TO AMOUNTS OF ILEUM RESECTED

	Ileostomy fluid						
	24-Hour volume (ml)	Mean water concentration (%)	Sodium		Potassium		
Group			mEq/d	mEq/l	mEq/d	mEq/l	Na/K
Less than 9 cm of ileum resected	401±92	89·8±2·5	43±12	106±14	4·0±0·99	10·3±2·4	10·8±2·4
30–120 cm of ileum resected	1202±284	93·1±1·8	146±53	119±23	12·7±9·0	11·1±9·9	15·6±7·7
*P**	<0·001	<0·001	<0·001		<0·001		<0·02

* *P* value given only when significant change occurred.
Results given as mean ±s.d.

of the low volume ileostomy, which we have described for a larger group of patients elsewhere (Hill, Mair and Goligher, 1975a). The faecal output, which was small at first, increased rapidly until the sixth postoperative day when a steady state was reached. The mean 24-hour faecal volume for days 7–12 after operation was 620 ± 44 ml and remained at 596 ± 67, 546 ± 67 and 530 ± 27 ml at 1, 6 and 12 months respectively. The daily faecal output of sodium and potassium similarly remained constant over the period of the study. There was, however, a marked fall in the water content of the ileostomy fluid between the first and second postoperative weeks (95·8 ± 2·9 per cent to 90·9 ± 0·63 per cent, $P < 0·005$). After 1 month the water content of the ileostomy fluid had fallen further (90·0 ± 0·63 per cent to 87·0 ± 58 per cent, $P < 0·001$), but thereafter there was no further significant change, with the percentage of water in the ileostomy fluid remaining between 87 and 89 per cent for up to 1 year. After the ileostomy volume had become stable the Na/K ratio in the fluid remained constant at around 12.

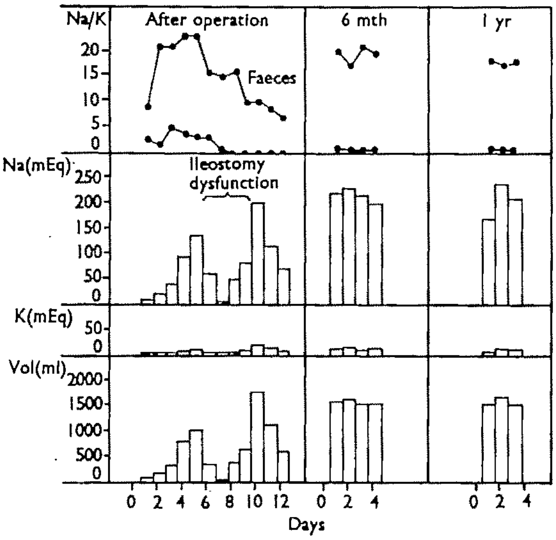


Fig. 2. Ileostomy chemistry in *Case* 10 measured at intervals over a 1-year period dating from the day of operation.

High volume output ileostomy: *Fig.* 2 describes the ileostomy function of *Case* 10 who was likewise followed from the immediate postoperative period at intervals for up to 1 year. At no time was he on steroid hormones. He provides a typical example of the ileostomy function found in a high volume type of ileostomy with an ileal resection (Hill, Mair and Goligher, 1975a). From the outset the faecal volume and output of sodium and potassium were higher than in the low volume ileostomy case. This higher output persisted over the 12-month study period (*Fig.* 2). The mean 24-hour faecal volume during the second postoperative week was 1011 ± 541 ml. At 6 and 12 months the daily faecal volume was 1590 ± 71 and 1543 ± 95 ml respectively. Although there was a significant fall in the water content of the ileostomy fluid between the first and second postoperative weeks (98·0 ± 0·6 per cent to 96·5 ± 22 per cent, $P < 0·025$), the water content did not fall further and remained around 95 per cent when measured at intervals up to 12 months.

The Na/K ratio in the ileostomy fluid was considerably higher than in the low volume group and was always above 15 apart from the second postoperative week when it fell concomitantly with the urine Na/K ratio, which was very low during this period.

Examination of *Fig.* 2 shows a marked reduction in volume and sodium output from days 6 to 9 in the postoperative period. During this time the patient had cramp-like abdominal pain and he provided a typical example of ileostomy dysfunction (Warren and McKittrick, 1951) from which he quickly and spontaneously recovered.

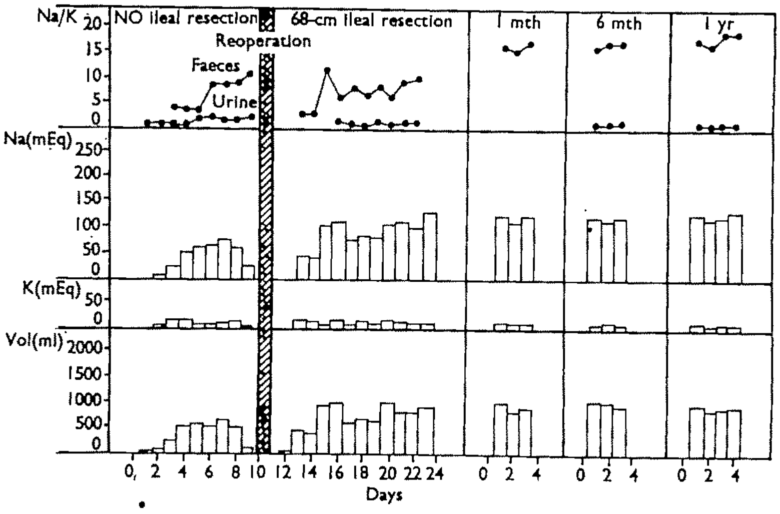


Fig. 3. Ileostomy chemistry in *Case* 11 measured at intervals over a 1-year period dating from the day the ileostomy was first established.

Low volume output ileostomy changing to high volume output ileostomy after secondary ileal resection: *Fig.* 3 describes the changes in ileostomy function in *Case* 11. He underwent proctocolectomy and ileostomy on 15 March 1973 for extensive ulcerative colitis. No ileal resection was performed at this operation and macroscopically and microscopically the ileal mucosa appeared normal. The operative period was covered by hydrocortisone administration 100 mg every 6 hours, and the dosage was then reduced rapidly until the eighth postoperative day when the dosage was 25 mg every 6 hours.

During the first postoperative week ileostomy function in this patient was typical for the low volume ileostomy. By the fourth postoperative day the 24-hour faecal volume was 530 ml and the daily volume remained within this range until the ninth postoperative day, when the patient developed severe abdominal pain and fever and the ileostomy ceased to function. On the tenth postoperative day lower abdominal tenderness developed and the perineal wound appeared tense and painful. The hydrocortisone dosage was returned to 100 mg every 6 hours and he was transferred to the operating room where laparotomy revealed that the ileum was caught up in the perineal wound and perforated in two areas, but there was no generalized intra-abdominal septic process. The terminal 68 cm of ileum, containing the perforated areas, were resected, the ileostomy was re-established in the right iliac fossa and the wound was closed. Subsequently the patient made an uninterrupted recovery and the hydrocortisone was reduced rapidly as after the primary operation and was discontinued by the end of the second postoperative week.

Following this second procedure in which 68 cm of terminal ileum were removed, ileostomy function assumed the character of a high volume ileostomy: On each postoperative day the ileostomy volume was larger than the corresponding day after the first procedure. The mean 24-hour faecal volume from days 4 to 8 after the first operation was 568 ± 52 ml, which was considerably smaller than the mean 24-hour faecal volume for the same period after the ileal resection (794 ± 178 ml, $P<0{\cdot}025$). At 1 month the daily faecal volume was 977 ± 126 ml, at 6 months it was 1033 ± 49 ml and it was 975 ± 76 ml at 1 year. At 1 year the water content (93 per cent) daily sodium output (130 mEq) and daily potassium output (7 mEq) were characteristic of a high volume ileostomy. The Na/K ratio remained consistently greater than 15 after the first month.

Effect of codeine and salt on the high volume ileostomy: *Table III* shows the effect of codeine phosphate alone and the effect of codeine phosphate and salt on ileostomy function in *Cases* 10 and 11. In both patients codeine phosphate caused a reduction in the daily faecal volume, which in one of them achieved statistically significant proportions. Addition of salt together with the codeine did not alter the faecal output. In both patients the water content of the ileostomy fluid fell and this reduction continued after the addition of salt.

In both patients there was a striking fall in ileostomy output of sodium and this persisted after the addition of salt. There was no change in the concentration of sodium in the ileostomy fluid in either patient during the study. Daily ileostomy excretion of potassium fell with codeine administration and this fall persisted after the administration of salt.

Fig. 4 illustrates these changes as seen in *Case* 10, and also shows the changes in the Na/K ratio in both the ileostomy fluid and the urine. *Case* 10 had been taking codeine phosphate tablets as an outpatient prior to admission to the metabolic ward for the study. *Fig.* 4 shows that the effect of this codeine was still apparent on day 1 of the study. The faecal volume was low, the faecal Na/K was low at 12·5 and he was in satisfactory sodium balance with a urine Na/K of 1·9. By the fourth control day (off all medication) his

Table III: EFFECT OF CODEINE AND SALT ON ILEOSTOMY OUTPUT IN CASES 10 AND 11

	Ileostomy fluid						
	24-Hour volume (ml)	Mean water concentration (%)	Sodium		Potassium		
Period			mEq/d	mEql	mEq/d	mEq/l	Na/K
Case 10							
Control (1)	1485±304	95·0±0·82	187±40	125±9	12·2±2·3	8·5±1·6	15·4±2·9
Codeine (2)	1085±53	92·8±0·96	131±7	120±3	11·8±1·0	10·8±0·43	11·2±0·3
Codeine and salt (3)	1035±210	93·5±1·3	127±21	123±8	8·7±1·8	8·6±2·0	14·9±3·3
P							
1 and 2	<0·05	<0·02	<0·05			<0·05	<0·05
2 and 3					<0·025		
1 and 3			<0·05		<0·05		
Case 11							
Control (1)	975±76	92·5±0·58	130±9	133±2·9	7·1±0·6	7·3±0·6	18·4±1·6
Codeine (2)	815±109	91·8±0·96	111±17	136±7·1	6·2±1·1	7·6±0·31	18·0±1·6
Codeine and salt (3)	665±59	91·0±1·8	89±11	134±7·8	5·3±0·9	8·0±0·7	16·8±13
P							
1 and 2							
2 and 3							
1 and 3	<0·001		<0·001		<0·02		

* *P* value given only when significant changes occurred.
Results given as mean ± s.d.

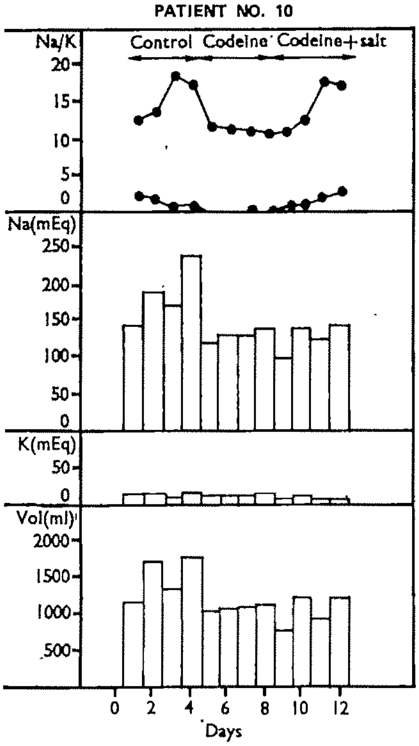


Fig. 4. Day-to-day changes in ileostomy chemistry in *Case* 10 during a control period, after the administration of codeine phosphate and after the administration of salt tablets together with codeine phosphate.

faecal volume had risen from 1150 ml on day 1 of the study to 1790 ml and the faecal Na/K ratio had risen from 12·5 to 17·5. Urinary conservation of sodium was now seen with a Na/K ratio of 0·09. On days 5 and 6 sodium disappeared from the urine.

After the administration of codeine phosphate the daily faecal volume fell within 24 hours to 1010 ml, and the consequent fall in sodium output from the ileostomy resulted in a reappearance of sodium in the urine, although the Na/K ratio remained low at 0·05.

After the administration of salt together with codeine phosphate the daily faecal volume remained low although the faecal Na/K rose, but this was due to a fall in potassium excretion rather than a rise in sodium excretion. Only after taking salt for 2 days did the urine Na/K ratio rise above 1, and by day 12 the Na/K ratio of 2·47 demonstrated good sodium balance.

Discussion

It is widely appreciated that if a significant amount of ileum is resected at the time of an ileostomy the output from the resulting ileostomy tends to be unusually profuse. A more accurate examination of the relationship between the amount of ileum resected and the amount of ileostomy output has been conducted by Nuguid et al. (1961). The present study affords still further precise confirmation of the role of ileal resection in increasing the amount of ileostomy effluent. This is shown in *Tables I* and *II* and in particular by *Fig.* 3, which demonstrates how in *Case* 11 a 'low volume ileostomy' was converted to a 'high volume ileostomy' after 68 cm of ileum were resected at a subsequent operation. Admittedly, it might be objected that the group of patients in our series with low output from their ileostomy was not strictly comparable with the group with high output, because in the latter there was a preponderance of males and the average age was less. There is, however, no strong evidence that men have on average higher output from their ileostomy than do women, and in the present study the tallest man (*Case* 6) had one of the lowest faecal outputs, whilst one of the smallest and oldest women (*Case* 12) had a large faecal volume.

How ileal resection results in a raised ileostomy is not fully understood. An obvious explanation is that it does so simply by loss of a significant amount of absorptive intestinal mucosa known to be important in the net transport of fluid and sodium (Hill, Mair and Goligher, 1975a), but since oral administration of bile salts increases the ileostomy output (Miettinen and Peltokallio, 1971) it is possible that the large volume of ileostomy effluent associated with ileal resection is a consequence of high bile salt concentration in the ileostomy fluid. Evidence that high concentrations of bile salts are present in some patients with an ileostomy has been provided by Miettinen and Peltokallio (1971), and there is nearly twice the incidence of gallstones in ileostomy patients who have had an ileal resection (Hill, Mair and Goligher, 1975b), suggesting an increased excretion of bile salts in such patients.

Many different drugs have been used to decrease ileostomy volume and sodium loss. Newton (1973) studied the effect of codeine phosphate, Lomotil and Isogel on ileostomy output of subjects living a normal life. It was concluded that codeine phosphate decreased the loss of sodium, potassium and water and that Lomotil had a similar but less pronounced action. Isogel, however, actually increased ileostomy volume and output of sodium and potassium. The present study confirms the beneficial effect of codeine phosphate, which effectively reduced ileostomy volume and sodium and potassium loss in 2 patients with a high volume ileostomy.

Sodium chloride given intravenously in the form of normal saline results in an increased volume of ileostomy output, but this response is not seen in patients who have had an ileal resection (Clarke and Hill, 1966; Hill, Mair and Goligher, 1975a). Orally administered sodium chloride also increases the volume of ileostomy effluent, but this effect is not marked until the total salt in the diet is 15 g or more a day (Kramer, 1966). It might be expected, therefore, that since the effect of oral and intravenous salt appears to be similar, patients with ileal resection might tolerate more oral salt without increased ileostomy output. Our clinical experience is consistent with this hypothesis, for in 2 patients when a daily dose of 8 g of sodium chloride was given orally over and above their usual dietary intake, there was no increased ileostomy output and the rise in the urine Na/K ratio showed a return to normal sodium balance.

Based on these studies and on clinical experience of a large number of other cases with a properly acting ileostomy, we have formulated a programme of management for patients who present with a high output ileostomy.

First of all, it should be pointed out that not every patient with an overactive ileostomy recognizes that he is different from other ileostomists. He may mention that he empties his ileostomy bag six or more times daily and has more than the usual trouble with leakage. There may be some complaint of occasional dizziness or light headedness from salt depletion or from excessive tiredness. If these manifestations are recent or associated with crampy abdominal pains, fever, weight loss or abdominal distension, the patient should be fully investigated for recurrent disease, intestinal obstruction or intra-abdominal sepsis.

After a thorough general physical examination the ileostomy is inspected and palpated with a finger for stricture. A specimen of ileostomy fluid and urine are sent to the laboratory for chemical analysis. A small bowel meal radiological study is then ordered and possibly an oral cholecystogram as well.

After recurrent disease, small bowel obstruction, intra-abdominal sepsis and chronic dietary indiscretion have all been excluded, there remains a group of patients in whom no specific cause for the high ileostomy output can be found. It is our experience that these patients have nearly always had an ileal resection. Characteristically, the ileostomy fluid appears watery and the Na/K ratio in the ileostomy fluid is greater than 15 whilst that in the urine is less than 1. Very rarely the patient with an ileal resection can have a faecal Na/K ratio of less than 5, but this is usually seen only in the early postoperative period or in very severe salt depletion (Clarke et al., 1967). In salt depletion of this magnitude sodium is absent from the urine. Although more elaborate and time-consuming 24-hour faecal and urine collections may be performed, we rely heavily in outpatient assessment on the simple measurement of the concentration and sodium and potassium in random specimens of ileostomy fluid and urine and on the calculation of the Na/K ratios. If the faecal Na/K ratio is below 15 and the urine Na/K ratio is greater than 1, the patient can be presumed to have satisfactory ileostomy function.

When the diagnosis of a high volume salt-losing ileostomy has been established, we commence the patient on 30–60 mg codeine phosphate every 6 hours and 2 g of salt every 6 hours. In 1 week's time he is seen again and questioned about his faecal output. Satisfactory reduction in volume is indicated by a reduction in the number of times he empties his bag (should be less than four to five times daily), and satisfactory sodium balance is indicated when the urine Na/K ratio rises above unity.

It is our experience that if the ileostomy overactivity is due entirely to ileal resection and is unassociated with any other abnormality it can usually be controlled by these means. If the codeine phosphate should cause side effects or prove ineffective, Lomotil is used as a substitute or supplement. It is not often necessary for the dose of codeine phosphate to be above 60 mg every 6 hours, but on occasion this becomes necessary and we do not hesitate to raise the dose considerably higher. Adequate control of the ileostomy volume with codeine phosphate rarely necessitates additional salt above 9 g/day, at which point the salt itself may result in an increased ileostomy output.

We wish to stress, however, that in the rare patients who do not respond to this regimen and whose ileostomy volume does not fall or falls only intermittently and in whom the urine Na/K remains less than 1 and the faecal Na/K is high (20 or more), the possibility that some pathological process of the small intestine may be causing the ileostomy dysfunction should be reconsidered and a full investigation undertaken. In some particularly difficult patients of this type we have exceptionally resorted to laparotomy as a further diagnostic step when all other investigations have proved unhelpful or inconclusive.

References

CLARKE A. M., CHIRNSIDE A., HILL G. L., POPE G. and STEWART M. K. (1967) Chronic dehydration and sodium depletion in patients with established ileostomies. *Lancet* **2**, 740–743.

CLARKE A. M. and HILL G. L. (1966) The effect of intravenous salt loading on fecal volume and electrolyte content in patients with ileostomies. *Proc. Univ. Otago Med. Sch.* **44**, 51–53.

CLARKE A. M., HILL G. L. and MACBETH W. A. A. G. (1967) Intestinal adaptation to salt depletion in a patient with an ileostomy. *Gastroenterology* **53**, 444–449.

GALLAGHER N. D., HARRISON D. D. and SKYRING A. P. (1962) Fluid and electrolyte disturbances in patients with long established ileostomies. *Gut* **3**, 219–223.

HILL G. L., GOLIGHER J. C., SMITH A. H. and MAIR W. S. J. (1975) Long term changes in total body water, total exchangeable sodium and total body potassium before and after ileostomy. *Br. J. Surg.* **62**, 524–527.

HILL G. L., MAIR W. S. J. and GOLIGHER J. C. (1975a) Impairment of ileostomy adaptation in patients after ileal resection. In preparation.

HILL G. L., MAIR W. S. J. and GOLIGHER J. C. (1975b) Gallstones after ileostomy and ileal resection. *Gut*. Awaiting publication.

KRAMER P. (1966) The effect of varying sodium loads on the ileal excreta of human ileostomized subjects. *J. Clin. Invest.* **45**, 1710–1718.

KRAMER P., KEARNEY M. M. and INGELFINGER F. G. (1962) The effect of specific foods and water loading on the ileal excreta of ileostomized human subjects. *Gastroenterology* **42**, 535–545.

MIETTINEN T. A. and PELTOKALLIO P. (1971) Bile salt, fat, water and vitamin B_{12} excretion after ileostomy. *Scand. J. Gastroenterol.* **6**, 543–552.

NEWTON C. R. (1973) The effect of codeine phosphate, Lomotil and Isogel on ileostomy function. *Gut* **14**, 424–425.

NUGUID T. P., BACON H. E. and BOUTWELL J. (1961) An investigation of the volume of output and chemical content of ileal discharge following total colectomy and ileostomy. *Surg. Gynecol. Obstet.* **113**, 733–742.

WARREN R. and MCKITTRICK L. S. (1951) Ileostomy for ulcerative colitis—technique, complications and management. *Surg. Gynecol. Obstet.* **93**, 555–567.

> AN honest workman not only surrenders his calm and peace once and for all, but must learn continually to jettison the form which his labour or art or thought first took, and go in search of new forms. To pause, so as to bask in or possess results, would be a betrayal of action. Over and over again he must go beyond himself, tear himself away from himself, leaving behind him his most cherished beginnings.
>
> TEILHARD DE CHARDIN. *Le Milieu Divin.* Reprinted: 1960, London, Collins; 1969, London, Fontana.

DISPRAY 1
Quick Prep
Chlorhexidine Gluconate 0.5% w/v in 70% I.M.S.
Stuart Pharmaceuticals Limited, Cheadle, Cheshire.
DISPRAY 2
Hard Surface Disinfectant

DISPRAY 1
TRADE MARK
Quick Prep
Chlorhexidine Gluconate 0.5% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for skin disinfection

'Dispray' 1 Quick Prep.
(formerly known as Hibispray 1)
is an ideal preparation for skin and
hand disinfection in the busy
hospital environment.
At the touch of a button it gives
fast, easy and economical
skin disinfection prior to surgery,
injection or venepuncture.
When colour delineation
is required eg. pre-operatively,
'Dispray' 3 is available
with a red dye.

The 'Dispray' range
combines effectiveness with
convenience and economy.

Instant Availability.
No solutions to prepare.

Easy to use.
No swabs or bottles required.

Quick and Effective.
Rapid bactericidal action.

Efficient Application.
No wasted solutions.

Contents cannot
be contaminated.
No rejected solutions.

Long Lasting.
Contents of one can treat 100sq.ft.

'Dispray' 1, 2, 3.
The Pick of the Bunch
for Disinfection.

DISPRAY 2
TRADE MARK
Hard Surface
Disinfectant
Chlorhexidine Gluconate 0.02% w/v
in 70% Industrial Methylated Spirit.

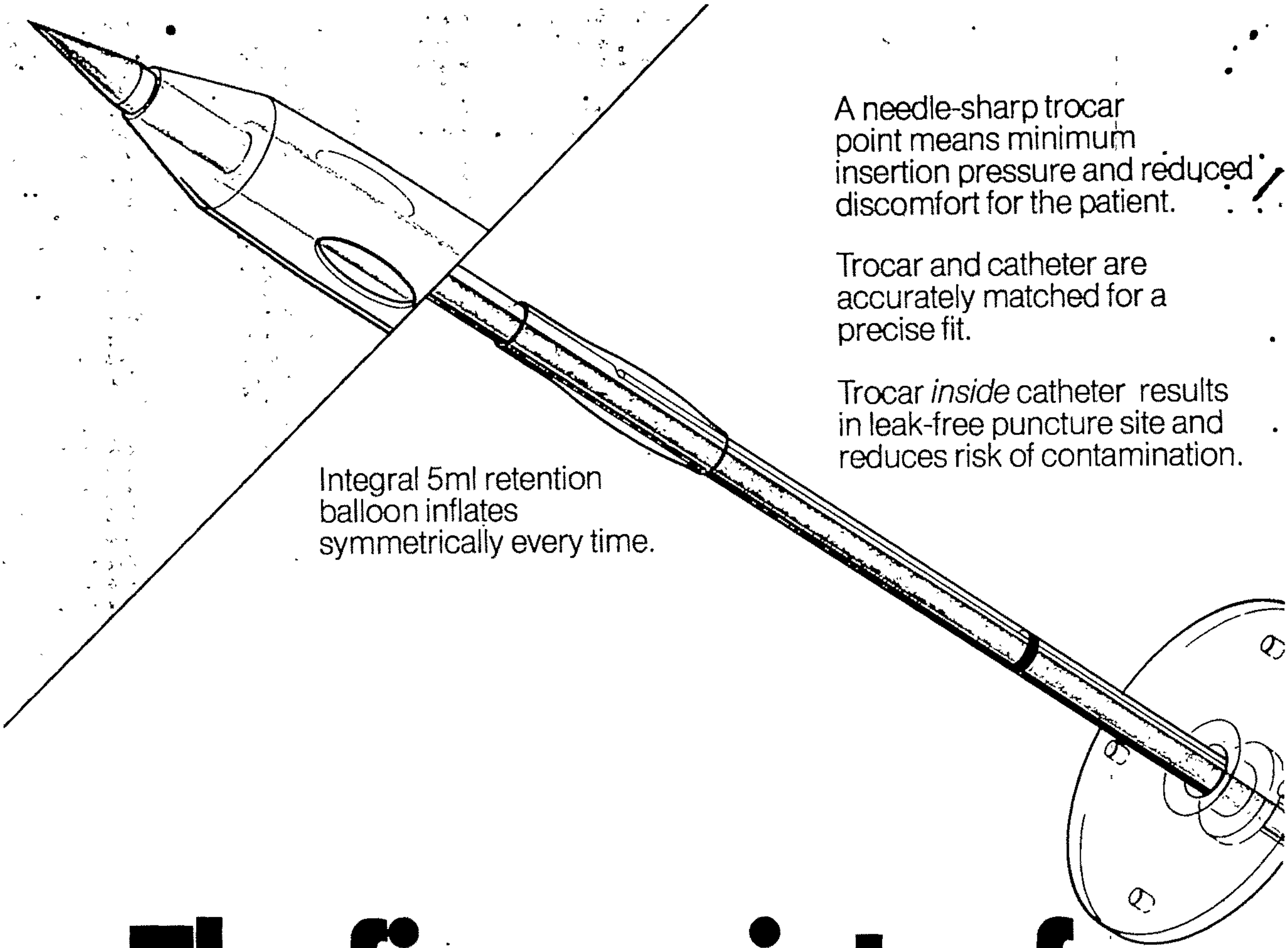
The pick of the bunch for hard surface disinfection

'Dispray' 2 Hard Surface
Disinfectant (formerly known as
Hibispray 2) provides rapid
disinfection of all hard surfaces
throughout the hospital.
Trolleys, cabinets, cupboards,
working surfaces – even footwear,
are rapidly, effectively
and efficiently disinfected.

Further
Information
is available
from:

STUART

Stuart
Pharmaceuticals
Limited,
Carr House,
Carrs Road,
Cheadle,
Cheshire SK8 2EG.



A needle-sharp trocar point means minimum insertion pressure and reduced discomfort for the patient.

Trocar and catheter are accurately matched for a precise fit.

Trocar *inside* catheter results in leak-free puncture site and reduces risk of contamination.

Integral 5ml retention balloon inflates symmetrically every time.

The finer points of a suprapubic catheter.

Our precisely engineered trocar and catheter combines maximum efficiency in operation with ease of use.

Check these points and see for yourself.

Sherwood MEDICAL INDUSTRIES

Sherwood Medical Industries Limited, London Road, County Oak, Crawley, West Sussex RH10 2

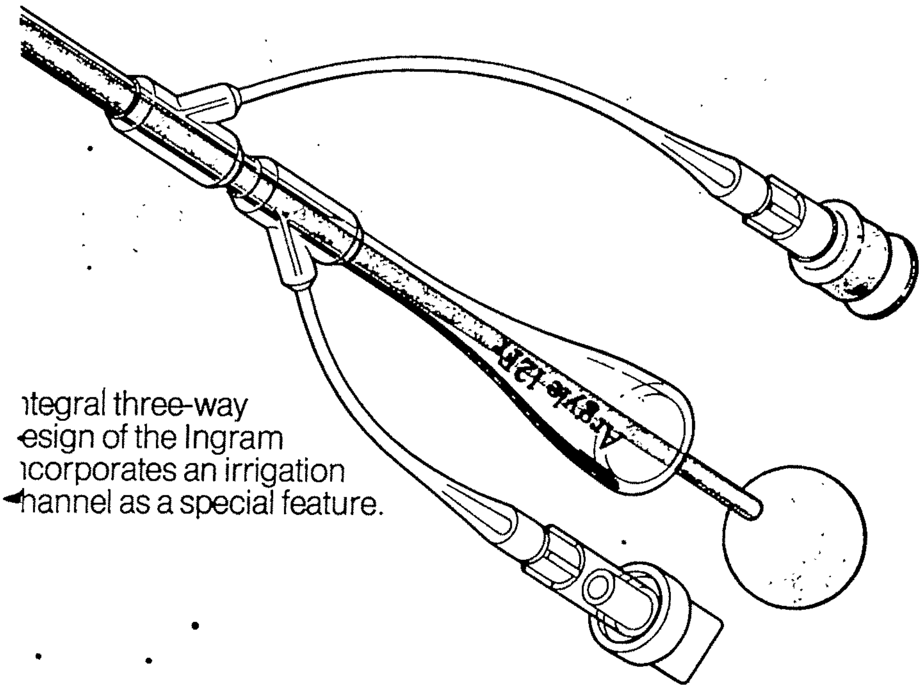
Tip, bevel, eyes. All ultra-smooth, all designed to minimise tissue damage.

Exclusive X-ray opaque Sentinel Line and Eye assists accurate location and positioning of catheter.

Available in both 12Ch and 16Ch sizes. Each unit packed in a convenient peel-back sterile tray.

liding plastic collar enables
atheter to be firmly
xed to maintain position.

nflation channel located inside
ne catheter wall. Drainage lumen
is therefore unobstructed.



ntegral three-way
esign of the Ingram
ncorporates an irrigation
hannel as a special feature.

OR SAFE, EFFICIENT
RINARY DRAINAGE

ARGYLE

NGRAM TROCAR CATHETER

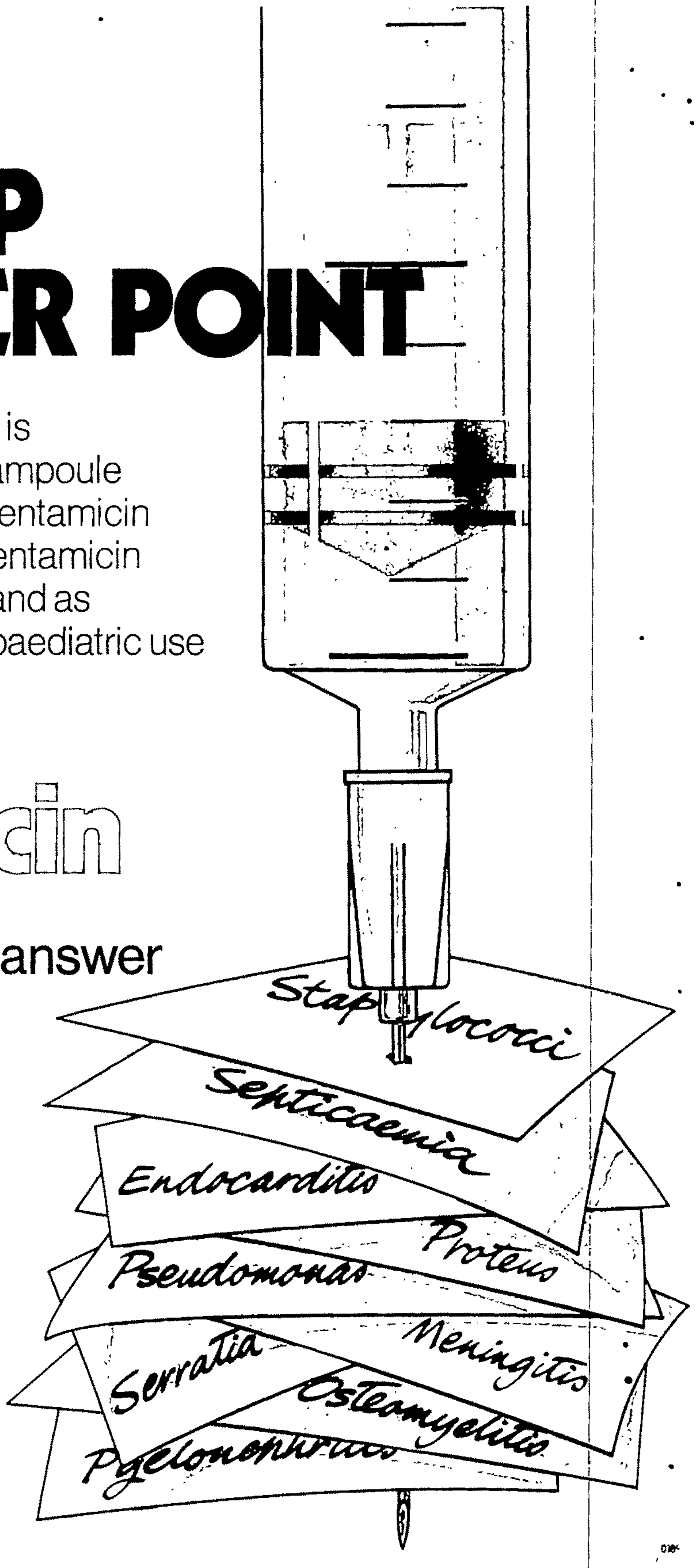
talogue Nos. MAR 5670–12 (12Ch) MAR 5670–16 (16Ch) 'Argyle' is a trade mark.

THE ARGYLE INGRAM TROCAR CATHETER
Please send me full technical literature ☐
Ask your representative to call ☐

Name BLOCK CAPITALS PLEASE
Address
Signature

THE
2 ML AMP
POWER POINT

Genticin Injectable is supplied as a 2 ml ampoule or vial containing gentamicin sulphate≡80 mg gentamicin base for adult use and as a 10 mg/ml vial for paediatric use



Genticin
injectable
the systemic answer

Full prescribing information is available on request
Nicholas Laboratories Limited.
225 Bath Road, Slough SL1 4AU.

'Genticin' is a trade mark
P.L. 0188/5026 Genticin Injectable
P.L. 0188/5018 Genticin Paediatric
U.K. Patent No 1.021.401

Nicholas

Pharmaceuticals, Toiletries
Hospital Supplies

Br. J. Surg. Vol. 62 (1975) 727–730

Factors influencing local recurrence after abdominoperineal resection for cancer of the rectum and rectosigmoid

A. R. MOOSSA, P. C. REE, J. E. MARKS, B. LEVIN, C. E. PLATZ
AND D. B. SKINNER*

SUMMARY

One hundred and fifty-two patients who underwent abdominoperineal resection for cancer of the rectum and rectosigmoid are reviewed. Six physicians were selected to predict which of these patients would have a local recurrence. All the information available at the end of the operation was duplicated and submitted to the observers. None of the physicians was able to predict local recurrence significantly better than random. There were 31 local recurrences, i.e. an incidence of 20·4 per cent. Low level of tumour in the rectum, local spread into perirectal fat or serosa, lymph node involvement and age below 60 years at time of operation were the only factors that were statistically related to local recurrence. The strategy for careful follow-up of patients at risk is outlined and a plea is made for a controlled trial of postoperative radiotherapy.

LOCAL tumour recurrence after abdominoperineal resection for cancer of the rectum and rectosigmoid junction remains a difficult clinical problem. Some 10–20 per cent of the 37 000 new cases seen each year in the United States will develop local and/or regional node recurrence following surgical treatment. About 50 per cent of the patients with local failure do not have distant metastases and yet the quality and duration of their survival are adversely affected. Clearly, the ability to identify subgroups of individuals at high risk would be advantageous in the selection of patients for adjuvant therapy and in the planning of the postoperative follow-up régime.

We investigated the ability of the physician to predict which patient is going to have a local recurrence and also to elucidate the factors responsible for such local failure. The preliminary results on the first 74 patients studied have already been discussed (Ree et al., 1975).

Patients and methods

Between 1943 and 1972 at the Department of Surgery, University of Chicago, 152 patients underwent abdominoperineal resection for cancer of the rectum and rectosigmoid and survived the first 30 days after operation. They were all followed up until death or for a minimum of 2 years, so that the majority of recurrences could be detected. Six physicians were selected to predict which of these patients would have a local recurrence. There were two surgeons, two pathologists, one gastro-enterologist and one radiotherapist. All the information available at the end of the postoperative period was duplicated and each physician was given copies of reports on the proctoscopy, intravenous pyelogram, barium enema, operative report and surgical pathology report. They were asked to focus their attention on variables that might be related to local recurrence and to evaluate each patient according to six parameters—level of tumour in the rectum, histological grade of malignancy, Dukes' class, presence of tumour in resected margin, blood vessel invasion, lymphatic involvement. The observers worked independently of each other. The patient's actual outcome was recorded separately from the information in the charts and tumour registry records.

Table I: PREDICTION OF LOCAL RECURRENCE

	Observer					
	1	2	3	4	4	6
Cases predicted to have a local recurrence (% of total)	34	34	39	44	55	68
Local recurrence correctly predicted (%)	36	56	57	44	72	78

Table II: SITES OF LOCAL RECURRENCE

Site: Pelvis	No. of cases:	10
Perineum		13
Vagina		6
Abdominal wall		2
	Total	31

Results

None of the observers was able to predict local recurrence significantly better than random. The physicians who detected the largest number of recurrences also predicted the largest number (*Table I*).

From the charts we found that there were 31 local recurrences among the 152 patients, which is an incidence of 20·4 per cent. Thirteen were in the perineal region, 10 in the pelvis, 6 in the vagina and 2 in the anterior abdominal wall (*Table II*). The median time from operation to local recurrence was 8·5 months with a range of 2–89 months. Twenty-six of the 31 patients (84 per cent) presented with their local recurrence within 1 year of operation. The average survival after detection of recurrence was 15 months with a range of 2–51 months. Autopsy or

---

* Departments of Surgery, Radiology, Medicine and Pathology, The University of Chicago, The Pritzker School of Medicine, Chicago, Illinois.

Table III: RELATIONSHIP OF LEVEL OF PRIMARY TUMOUR TO INCIDENCE OF LOCAL RECURRENCE

Level of primary tumour	No. of cases	Local recurrence No.	%
Upper third of rectum and rectosigmoid junction	28	1	3·6
Middle third of rectum	42	4	9·5
Lower third of rectum	82	26	31.7
Total	152	31	20·4

$\chi^2 = 11·46$, $P<0·005$.

Table IV: RELATIONSHIP BETWEEN LOCAL SPREAD OF TUMOUR AND INCIDENCE OF LOCAL RECURRENCE

Local spread into perirectal fat or serosa	No. of cases	Local recurrence No.	%
Yes	30	17	56·7
No	122	14	11·4
Total	152	31	20·4

$\chi^2 = 30·3$, $P<0·001$.

Table V: RELATIONSHIP BETWEEN REGIONAL LYMPH NODE INVOLVEMENT AND INCIDENCE OF LOCAL RECURRENCE

Regional lymph node involvement	No. of cases	Local recurrence No.	%
Positive	70	22	31·4
Negative	82	9	11·0
Total	152	31	20·4

$\chi^2 = 9·73$, $P<0·005$.

Table VI: RELATIONSHIP BETWEEN AGE OF PATIENT AND INCIDENCE OF LOCAL RECURRENCE

Age at time of operation (yr)	No. of cases	Local recurrence No.	%
<60	61	20	32·8
>60	91	11	12·1
Total	152	31	20·4

$\chi^2 = 9·638$, $P<0·005$.

Table VII: RELATIONSHIP BETWEEN MUCIN PRODUCTION AND INCIDENCE OF LOCAL RECURRENCE

Mucin production by tumour	No. of cases	Local recurrence No.	%
Positive	25	7	28
Negative	127	24	19
Total	152	31	20·4

$\chi^2 = 1·066$, $P<0·5$.

Table VIII: RELATIONSHIP BETWEEN SEX AND INCIDENCE OF LOCAL RECURRENCE

Patient's sex	No. of cases	Local recurrence No.	%
Female	81	20	24·7
Male	71	11	15·5
Total	152	31	20·4

$\chi^2 = 1·972$, $P<0·2$.

Table IX: RELATIONSHIP BETWEEN DUKES' CLASSIFICATION AND INCIDENCE OF LOCAL RECURRENCE

Dukes' class	No. of cases	Local recurrence No.	%
A	5	0	0
B	76	13	17·1
C	66	18	27·2
Not classified	5	—	—
Total	152	31	20·4

$\chi^2 = 1·964$, $P<0·2$.

Table X: RELATIONSHIP BETWEEN HISTOLOGICAL GRADE OF MALIGNANCY AND INCIDENCE OF LOCAL RECURRENCE

Histological grade	No. of cases	Local recurrence No.	%
Well differentiated	58	11	19·0
Moderately well differentiated	46	8	17·4
Poorly differentiated	15	3	20·0
Total	119	22	18·5

$\chi^2 = 0·05562$.

Table XI: RELATIONSHIP BETWEEN PERFORATION OF BOWEL WALL AND INCIDENCE OF LOCAL RECURRENCE

Perforation of bowel wall by tumour or surgeon	No. of cases	Local recurrence No.	%
Yes	25	5	20·0
No	127	26	20·4
Total	152	31	20·4

$\chi^2 = 0·0135$, $P = 0·995$.

Table XII: RELATIONSHIP BETWEEN VOLUME OF TUMOUR AND INCIDENCE OF LOCAL RECURRENCE

Volume of tumour in surgical specimen (ml)	No. of cases	Local recurrence No.	%
<10·0	45	9	20·0
>10·0	61	12	19·6
Total	106	21	19·8

$\chi^2 = 0·002$, $P>0·995$.

'second look' laparotomy data were available for 24 of the 31 patients. Only 13 of them had evidence of distant metastases.

The following factors were significantly related to local recurrence: low level of tumour in the rectum (*Table III*), local spread into perirectal fat or serosa (*Table IV*), lymph node involvement (*Table V*) and age below 60 years (*Table VI*). Mucin production by the tumour (*Table VII*), female sex (*Table VIII*) and Dukes' class (*Table IX*) showed a trend to local recurrence, but were not significantly related to it.

The following factors were unrelated to local recurrence: histological grade of malignancy (*Table X*), perforation of bowel by tumour or surgeon (*Table XI*), volume of tumour (*Table XII*) and the range of years when the operation was performed (*Fig.* 1).

Discussion

Over the past 30 years emphasis has been placed on earlier diagnosis of colorectal cancer. In spite of the intensive public education programmes and thorough investigations using endoscopy and cytological and radiological techniques, the relative incidence of the different stages of the disease has remained unaltered. The survival rates have improved but slightly. Most of the benefit can be accounted for by an increase in resectability rate with a lower operative mortality. The results of a 'curative resection' for each stage of the disease have remained virtually unchanged (Polk et al., 1973).

Opinions vary on the exact cause of mortality and morbidity following abdominoperineal resection for rectosigmoid cancer. Dionne (1965) believed that nearly all patients with colorectal carcinoma die as a result of venous spread of the disease. Our limited data do not support this contention. The majority of our patients with recurrent colorectal cancer died from local problems. This is borne out by the study of Floyd et al. (1965), who found that local tumour spread was the major cause of death in 25 of their 34 patients. The extensive post-mortem examinations carried out by Taylor (1962) demonstrated that in 75 per cent of his 125 patients death was due to local persistence of the growth.

The implications of our study support the view of others (Gunderson and Sosin, 1974) that the use of radical surgery as has been practised over the past 10 years does not necessarily prevent problems with local failure. The majority of recurrences occur within the first year after surgery, and this suggests that they are derived from microscopic or subclinical 'residual' tumour left during 'curative' operative attempts. Further, the high percentage of local recurrence in our group of patients cannot be attributed to the use of sphincter-saving procedures.

Our data show some unexpected trends which may be partially due to the small number of patients in our series. We have not confirmed the report of Morson et al. (1963) that the degree of histological differentiation is a prognostic factor for local recurrence. The higher incidence of local failure in women may be explained by the tendency of our surgeons to preserve the vagina. The biologically more aggressive rectosigmoid tumours in the young cannot be accounted for on the available data. We have not looked at other potentially important parameters such as germinal centre activity and sinus histiocytosis in lymph nodes and the presence of local wound sepsis.

The incidence and pattern of 'residual' or 'recurrent' cancer after abdominoperineal resection can be predicted fairly accurately if the basic anatomy of the rectum and pelvis, the pathologic extent of the primary lesion and the limitations of surgical technique are kept in mind. We believe that patients under the age of 60 years belonging to Dukes' classes B_2, C_1 and C_2 (Astler–Coller modification, 1954) who had the primary lesion at or below the peritoneal reflection should be included in a prospective random study of postoperative irradiation. The eligible patients in such a trial should be protected from unnecessary irradiation. The upper extent of the field should be based on the type of operative procedure and the degree of tumour involvement. Probably patients with local tumour spread should only receive irradiation to the lesser pelvis, while those with nodal metastases should receive additional treatment to the aorto-iliac and hypogastric nodal basins.

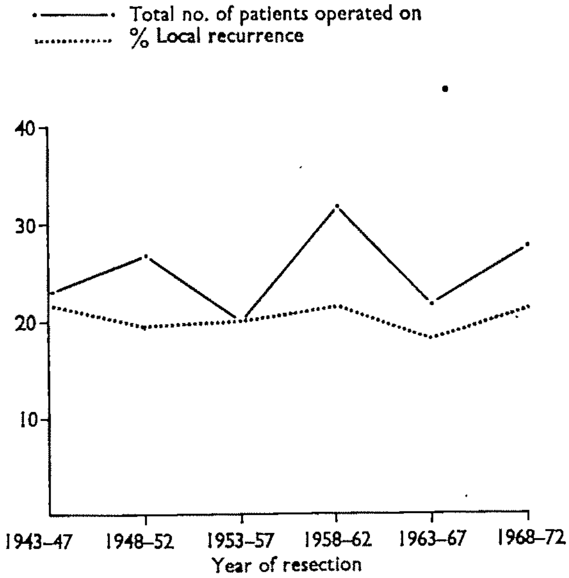


Fig. 1. Relationship between range of years when the operation was performed and incidence of local recurrence.

The strategy for postoperative follow-up of the patients at risk should be stringent during the first postoperative year (Ree et al., 1975). Careful perineal and vaginal examination is mandatory. Any residual sinus tract in the perineum should be probed and curetted and the material sent for histological diagnosis. The curative benefit of routine 'second look' laparotomy is dubious (Gunderson and Sosin, 1974). However, patients with suggestive symptoms, especially perineal or sacral pain, should be carefully evaluated and re-explored with a view to locating residual tumour early and excising the bulk of the recurrence. They could then be randomized in some adjuvant therapy protocol. The role of serial determinations of the carcino-embryonic antigen in selecting patients for reoperation is being currently investigated at our institution.

We have demonstrated that physicians are not always able to predict cases of rectosigmoid carcinoma in which local recurrence will appear following surgery. This does not imply that a *laissez-faire* attitude should prevail. The general pessimistic outlook regarding recurrent colorectal cancer is unjustifiable and the exact extent of these recurrences should be fully assessed (Polk and Spratt, 1971). Adjuvant therapy should be studied in detail to draw conclusions regarding improved tumour control and the complications of retreatment.

Acknowledgements

We are grateful to Mrs Lowenstein of the Tumour Registry Record for supplying all the relevant data, and to Dr A. W. Hall and Mrs Arlie Jones for their help in the preparation of this manuscript.

References

ASTLER V. B. and COLLER F. A. (1954) The prognostic significance of direct extension of carcinoma of the colon and rectum. *Ann. Surg.* **139**, 846–851.

DIONNE L. (1965) The pattern of blood borne metastasis from carcinoma of the rectum. *Cancer* **18**, 775–781.

FLOYD C. E., CORLEY R. G. and COHN I. jun. (1965) Local recurrence of carcinoma of the colon and rectum. *Am. J. Surg.* **109**, 153–159.

GUNDERSON L. L. and SOSIN H. (1974) Areas of failure found at reoperation (second or symptomatic look) following 'curative surgery' for adenocarcinoma of the rectum. *Cancer* **4**, 1278–1292.

MORSON B. C., VAUGHAN E. G. and BUSSEY H. J. R. (1963) Pelvic recurrence after excision of rectum for carcinoma. *Br. Med. J.* **2**, 13–18.

POLK H. C., AHMAD W. and KNUTSON C. O. (1973) Carcinoma of the colon and rectum. In: *Current Problems in Surgery*. Chicago, Year Book, pp. 1–64.

POLK H. C. and SPRATT J. S. (1971) Recurrent colorectal carcinoma: detection, treatment and other considerations. *Surgery* **69**, 9–23.

REE P. C., MARKS J. E., MOOSSA A. R., LEVIN B. and PLATZ C. E. (1975) Rectal and rectosigmoid carcinoma: physician's prediction of local recurrence. *J. Surg. Res.* **18**, 1–7.

TAYLOR F. W. (1962) Cancer of the colon and rectum—a study of routes of metastases and death. *Surgery* **52**, 305–308.

Br. J. Surg. Vol. 62 (1975) 731–733

The transdiaphragmatic approach to the heart

E. W. J. CAMERON*

SUMMARY

A modification of the transdiaphragmatic approach to the heart is described. The technique has been used successfully in both adults and children, the youngest child being 8 years of age. The approach has advantages over others in gaining access to the heart for purposes of internal cardiac massage and drainage of suppurative pericarditis and is also a suitable manœuvre in the surgical treatment of acute tamponade. Clinical experience in the use of this approach is summarized. The transdiaphragmatic approach is recommended as a standard technique for internal cardiac massage.

THE transdiaphragmatic approach to the heart was first advocated by Sauerbruch (Siddons, 1968), who used a transverse epigastric incision. Modern descriptions of the approach are remarkable for their rarity. In instances where acute tamponade occurs after a cardiac operation performed through a median sternotomy it is common practice to open first the inferior end of the incision, since this limited exposure often serves to evacuate the blood without having to separate the sternal fragments. Most other descriptions advise entry at the left xiphocostal angle through the rectus sheath (Belsey, 1968; Ebert, 1969; d'Abreu et al., 1971). This approach is complicated by the close relation of the superior epigastric vessels and the risk to the marginal artery which underlies the natural point of entry into the pericardium. An approach through the linea alba and peritoneal cavity has also been described (McNair, 1972). Here the left lobe of the liver must be freed by division of the left triangular ligament. There is also the problem of coping with the abdominal contents. Fitzgerald (1966) has evolved a transdiaphragmatic approach through a left subcostal incision. Again, the greater sophistication of the anatomy makes this route less favourable than that now to be described.

Technique

A vertical skin incision is made in the midline; the centre point of the incision is the tip of the xiphoid process. Superiorly the incision is carried anterior to the sternum and inferiorly to midway between the tip of the xiphoid process and the umbilicus. The incision is deepened to the sternal periosteum and through the linea alba to the peritoneum. The xiphoid process is bisected vertically after its deep surface has been cleared with a finger or a dissector. By a combination of blunt dissection and lateral retraction of the wound edges the peritoneum is separated from the abdominal surface of the central tendon of the diaphragm, and the central tendon is displayed. The tendon is then grasped with tissue forceps, lifted with the parietal pericardium from the surface of the heart and incised through to open the pericardial space. The diaphragmatic pericardium is firmly adherent to the central tendon and the two structures can be incised without preliminary elevation to allow quicker and equally safe entry to the pericardial space. The primary incision is widened to display the diaphragmatic and anterior surfaces of the heart.

Discussion

This modification of the transdiaphragmatic approach has the particular advantages that it is rapid and simple to perform, that no vessels, nerves or muscles are divided and that there is no need to open the pleural or peritoneal cavities. It is the inferior end of the incision for mid-sternal thoracotomy and can therefore be extended superiorly to give a general exposure of the heart. The only necessary instrument is a scalpel. For cardiac massage the hand and wrist of the operator lie in a comfortable position, the extended fingers of the right hand over the lateral aspect of the left ventricle, the thenar eminence and thumb over the right ventricle. This contrasts with the thoracic exposure through which, without a self-retaining retractor, cardiac massage is difficult and even painful for the operator. Access for internal electrical defibrillation is easy by the abdominal route. Also, a single operator can simultaneously massage the heart and ventilate the lungs by mouth-to-mouth or tube technique.

The main theoretical danger with this approach is that when the pericardium is opened either the myocardium or coronary vessels may be injured. Myocardial injury should be repairable. The threatened coronary vessels, the marginal and right coronary arteries and their accompanying veins, should be avoided by siting the primary incision in the central tendon to the right of the midline over the diaphragmatic surface of the heart. Injury to the inferior vena cava could be produced by an unnecessary posterior extension of the incision. The chance of any such injury is minimal, particularly when the heart is still. When the parietal and visceral layers of the pericardium are mutually adherent, urgent intrapericardial manipulation of the heart is in any event impossible and the chance of cardiac injury on incision of the central tendon increases—a difficulty common to both the abdominal and thoracic approaches. It is, however,

---

* Thoracic Surgical Unit, Wentworth Hospital, P. B. Jacobs, Natal, South Africa.

Present address: Department of Anatomy, University of Edinburgh.

easier to perform effective extrapericardial massage by the abdominal than by the thoracic route. Obliteration of the pleural space may present an obstacle to access by the thoracic route. The abdominal route which does not traverse a serous cavity avoids this.

The most widespread use of the transdiaphragmatic approach would be for internal cardiac massage (ICM). This manœuvre has been eclipsed by the success and simplicity of external cardiac massage (ECM). The theoretical and experimental evidence of the superiority of ICM over ECM in terms of cardiac output has been summarized by Stephenson (1969). Weale and Rothwell-Jackson (1962), in experiments on dogs, have also demonstrated venous systolic pulses of up to 60 mm Hg on ECM. This poses a threat of brain damage which does not occur with ICM. Visceral damage caused to patients, particularly the elderly, by ECM is well documented. There are reports of instances where cardiac standstill despite ECM has been converted to action by subsequent ICM (Paul, 1964). It is still widely taught that failure to resuscitate by ECM is an indication for ICM, and it is certain that evidence of inadequate perfusion by ECM, for example dilating pupils where ventilation is satisfactory, is an indication for ICM. There are well-recognized groups of patients which are unsuitable for ECM, particularly those suffering from cardiac tamponade or stove-in chest, after pneumonectomy or women in late pregnancy. A single operator cannot manage resuscitation where he has simultaneously to ventilate the patient and perform adequate ECM.

The transdiaphragmatic approach has been used in the management of 5 cases of cardiac arrest. In 2 of these resuscitation was successful, in 2 unsuccessful and in 1 cardiac action was restored following ICM but subsequently rearrested. No technical problems were encountered in carrying out the transdiaphragmatic procedure.

Case reports

Case 1: A 52-year-old man sustained bilateral pulmonary contusion and multiple rib fractures in a car accident. He was treated with intermittent positive pressure respiration and during this procedure the endotracheal tube blocked and the patient had a cardiac arrest. In view of the chest wall injuries, resuscitation was managed by ICM. The patient subsequently recovered.

Case 2: A 26-year-old man had a Starr-Edwards replacement of an aortic valve 14 days before the sudden onset of ventricular fibrillation. Potassium levels were normal. External defibrillation failed. Sinus rhythm returned after internal defibrillation, and the patient subsequently recovered. A fault in the lead of one of the external defibrillator paddles was later discovered.

Case 3: A 68-year-old man had a cardiac arrest 60 minutes after the development of an anterolateral myocardial infarction. He was kyphotic. ECM caused bilateral rib fractures. The heart was in asystole prior to attempting ICM, which in turn proved futile.

Case 4: A 43-year-old man sustained an anterolateral myocardial infarction. Three hours after the onset of chest pain and after multiple ventricular extrasystoles, ventricular fibrillation occurred, followed by asystole. There was no sign of cardiac recovery after 30 minutes' ECM during which the heart was needled on several occasions. ICM was equally ineffective. There was a haemopericardium containing an estimated 50 ml of blood consequent on earlier cardiac puncture.

Case 5: A 60-year-old woman, admitted with a posterior myocardial infarction 4 days previously, had a cardiac arrest. She was 1·6 m tall and weighed 72 kg. Perfusion was inadequate on ECM. Six minutes after starting ICM there was satisfactory cardiac action. Subsequently, the patient had multiple arrhythmias and the heart went into asystole 3 hours after the initial resuscitation. All further attempts at resuscitation, including ICM, failed.

Drainage of suppurative pericarditis by this route is simple and effective. It allows of dependent drainage, no tissue compartment is breached in gaining access to the pericardium and the whole of the pericardium can be easily reached. This method has been used in the management of 4 cases of staphylococcal pericarditis. The patients were children aged between 8 and 12 years. All presented with pyopericardium and tamponade after failure of medical management to control the infection. In 2 children pyopericardium recurred after initial drainage through a left anterior thoracotomy with resection of the sixth or seventh costal cartilages. These patients were then redrained using the transdiaphragmatic route. All 4 patients recovered after transdiaphragmatic drainage.

The use of the approach for the relief of acute tamponade after cardiac operations has been mentioned. It is an equally reasonable method for the relief of traumatic tamponade where there is clinical and radiological evidence of only cardiac injury. Two patients, men of 20 and 22 years of age, presented with precordial stab wounds and clinical evidence of cardiac tamponade, and the chest X-rays showed globular enlargement of the pericardium. The transdiaphragmatic entry into the pericardium rapidly relieved the cardiac embarrassment. The surgical incision was then extended superiorly to complete a midsternal thoracotomy, and wounds in the left ventricular myocardium and great cardiac vein respectively were sutured. Both patients subsequently recovered.

Siddons (1968) has described the use of a transdiaphragmatic approach through the anterior rectus sheath to implant the epicardial loop of a pacemaker system.

The transdiaphragmatic approach is valid for the relief of acute cardiac tamponade and has advantages over the intercostal route for ICM and drainage of suppurative pericarditis. ICM may be an under-used resuscitatory technique, in which case simplification and standardization of the surgical approach to the heart would encourage the appropriate use of ICM. The proposed modification of the transdiaphragmatic approach is therefore the surgical approach recommended for ICM.

Acknowledgements

I am grateful to Professor B. T. Le Roux and Mr Andrew Logan for encouragement and help with preparation of this paper.

References

D'ABREU A. L., COLLIS J. L. and CLARKE D. D. (1971) *A Practice of Thoracic Surgery*, 3rd ed. London, Arnold, p. 147.

BELSEY R. (1968) Pericardiectomy and drainage of the pericardium. In: ROB C. and SMITH R. (ed.) *Operative Surgery*, Vol. 2: *Thorax*, 2nd ed. London, Butterworths, p. 302.

EBERT P. A. (1969) The pericardium. In: GIBBON J. H., SABISTON D. C. and SPENCER F. C. (ed.) *Surgery of the Chest*, 2nd ed. Philadelphia, Saunders, p. 564.

FITZGERALD P. (1966) A subcostal approach to the heart. *Ir. J. Med. Sci.* **6**, 111–112.

MCNAIR T. J. (ed.) (1972) *Emergency Surgery* (*Hamilton Bailey*), 9th ed. Bristol, Wright, p. 81.

PAUL J. D. jun. (1964) Puerperal uterine rupture complicated by cardiac arrest. *Pa. Med. J.* **67**, 41–42.

SIDDONS A. H. M. (1968) Cardiac pacing. In: ROB C. and SMITH R. (ed.) *Operative Surgery*, Vol. 2: *Thorax*, 2nd ed. London, Butterworths, p. 347.

STEPHENSON H. E. (1969) *Cardiac Arrest and Resuscitation*, 3rd ed. St Louis, Mosby, pp. 242–248.

WEALE F. E. and ROTHWELL-JACKSON R. L. (1962) The efficiency of cardiac massage. *Lancet* **1**, 990–992.

Br. J. Surg. Vol. 62 (1975) 734–736

False abdominal aortic and iliac aneurysms

DEMETRIOS CHAVATZAS AND CRAWFORD JAMIESON*

SUMMARY

A case of late postoperative false abdominal aortic and iliac aneurysms complicated by malposition of the inferior vena cava is presented and attention is drawn to its presentation, diagnosis and management. Several factors assumed to be responsible for the formation of the false aneurysms 7 years after the previous grafting operation are discussed.

MAJOR aortic surgery began with the first resection of a saccular aneurysm of the aorta by Oschner in 1944 (Cooley and DeBakey, 1952), and in 1949 Swan et al. (1950) successfully excised a coarctation of the aorta with an associated aneurysm and replaced it with a homograft. Following the work of Voorhees et al. (1952), DeBakey et al. (1958), Martin (1963) and others, replacement of the human aorta by synthetic grafts has become standard practice, but problems still remain. We present a case of recurrent abdominal aortic and iliac aneurysms associated with malposition of the inferior vena cava, with emphasis on its presentation, diagnosis and management.

Case report

A 65-year-old man was admitted to Hammersmith Hospital complaining of a painful pulsatile mass in the lower abdomen over a period of 1 year. He also suffered from attacks of angina pectoris. Seven years previously abdominal aortic and bilateral iliac aneurysms had been resected with insertion of a Dacron bifurcation graft from 3 cm below the renal arteries to both external iliac arteries. A cholecystectomy for cholelithiasis had been performed at the same time. During the operation it had been noted that the inferior vena cava crossed from left to right anterior to the aneurysm. The patient had also had a myocardial infarction 8 years previously.

On general examination he was reasonably fit for his age, although obese, and his blood pressure was 180/100 mm Hg. Abdominal examination revealed a large tender pulsatile mass in the lower abdomen. The lower limb pulses were present and ultrasound studies showed ankle pressures of 130 mm Hg. Apart from slight ischaemic changes in the ECG, other routine investigations including haemoglobin, platelets, cholesterol, triglycerides and chest X-ray were normal. An arteriogram via a right femoral arteriotomy showed an aneurysmal right iliac artery poorly communicating with the lower abdominal aorta. The rest of the proximal and distal arterial tree was not visualized.

Via a wide transverse incision the peritoneal cavity was opened, and after a dissection made difficult by extensive fibrosis from the previous operation, a diffuse aneurysm of the right aorto-iliac region was seen (*Fig.* 1). Another large aneurysm with the sigmoid colon stretched over its surface filled the pelvis. The inferior vena cava crossed from left to right anterior to the aneurysm, and lateral to this a segment of the ileum was adherent to the wall of the aortic aneurysm. The aneurysm had eroded the ileal wall and rupture into the gut appeared imminent.

The inferior vena cava was divided and sutured just distal to the left renal vein in order to facilitate clamping and control of the neck of the aortic aneurysm (*Fig.* 2). The external iliac arteries were clamped and the aorta was clamped just distal to the renal arteries. After incision and evacuation of the aortic aneurysm the previously inserted graft (*Fig.* 3) was found to be loose and coiled in the pelvis; its proximal end was 15 cm from the point at which it had been sutured to the aorta. The prosthesis was removed. The segment of ileum attached to the wall of the aneurysm was freed together with a patch of thin aneurysmal wall. A new bifurcation graft was inserted from 1 cm below the renal arteries to the distal external iliac arteries (*Fig.* 4). The external iliac arteries were then ligated proximal to this graft. Since the pulse did not return in the pelvic aneurysm after flow was restored, both internal iliac arteries must have been thrombosed. The abdominal wound was closed in layers. Postoperatively, the patient suffered from reversible acute tubular necrosis and, as was expected, from bilateral leg oedema. Eventually, he recovered and was discharged home.

Discussion

It is known (Shatz et al., 1962) that in the presence of ischaemic heart disease, the patient is at risk of death from myocardial infarction as well as from rupture of his aneurysm, but our patient, though he suffered from angina pectoris, was clearly more at risk from rupture of the aneurysm into the ileum. This man, who was in his seventh decade with a history of myocardial infarction and aorto-iliac aneurysmectomies and suffering from ischaemic heart disease, responded satisfactorily to further abdominal and iliac aneurysmectomies 7 years after the first operation. This type of massive and multiple false aneurysm has not apparently been described in the British or American literature. More such cases will undoubtedly be seen in the future. Gastro-intestinal haemorrhage due to erosion into the gut, most commonly the duodenum, is now well documented (Shiel et al., 1969; Eastcott, 1973).

The cause of recurrent aneurysms and false aneurysms following arterial reconstruction for occlusive disease is not yet fully established. Sepsis may obviously contribute, but the great majority present late and in our and others' experience are sterile on bacterial culture. They are commonest in the femoral region, and the stress applied to the anastomosis of prosthesis to artery by movement of the hip joint has been advocated as a major cause (Stoney et al., 1965; Sawyers et al., 1967; Spratt et al., 1967). For this reason many surgeons attempt to avoid siting an anastomosis in the femoral artery. The reasons for this must be good, however, for a more proximal anastomosis is more difficult and also leaves a common site of recurrent stenosis in the common femoral artery distal to the reconstruction.

Much evidence has accumulated to incriminate silk sutures as a major cause of false aneurysm. Dacron

---

* Peripheral Vascular Unit, Department of Surgery, Hammersmith Hospital and Royal Postgraduate Medical School, London.

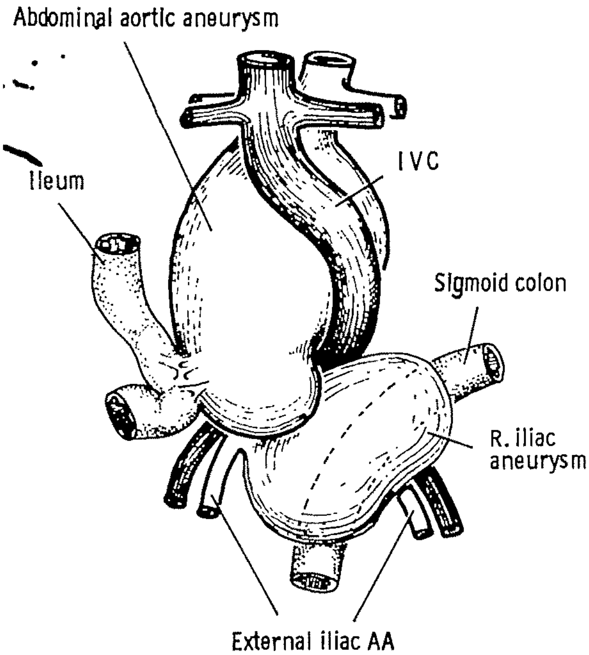


Fig. 1. Diagram of the aneurysms.

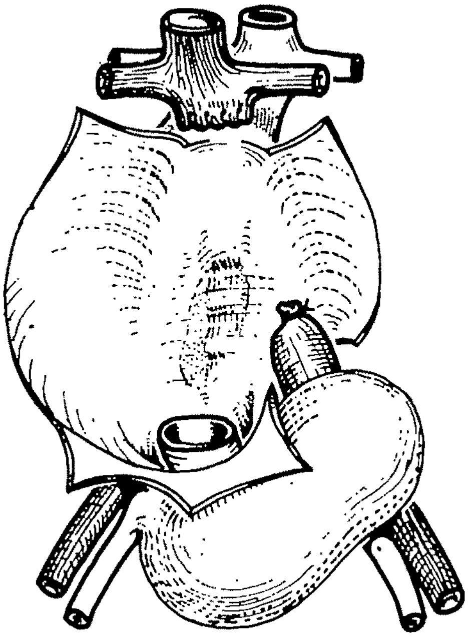


Fig. 2. Diagram showing the point of division of the inferior vena cava.

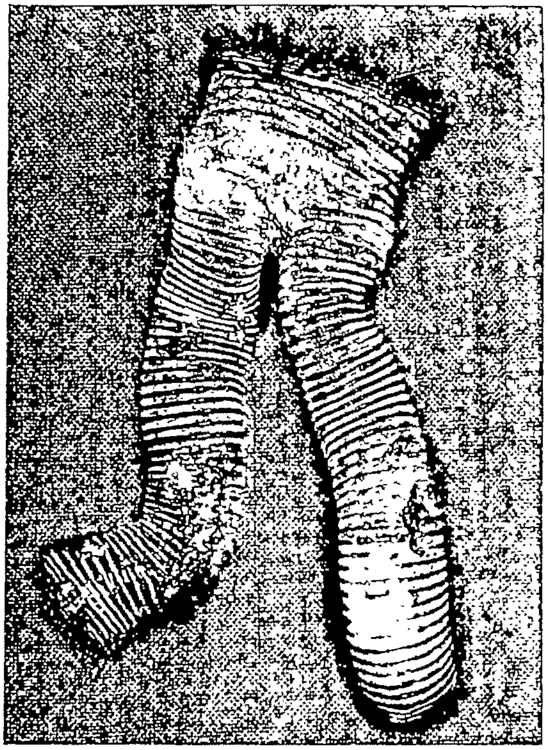


Fig. 3. The previously inserted graft which was found loose in the pelvis.

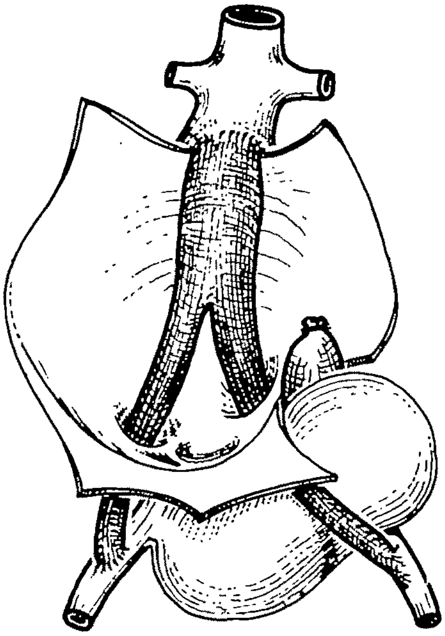


Fig. 4. Diagram showing the new graft position.

or Teflon never 'heals' satisfactorily to an artery and the integrity of the anastomosis probably depends indefinitely on its sutures. Silk loses its strength completely after a few years *in vivo* (Cutler and Dunphy, 1941), and most false aneurysms have been associated with its use (Moore and Hall, 1970). It is probable, therefore, that the employment of stronger synthetic suture materials will reduce the incidence of false aneurysms. There is also now a tendency for vascular surgeons to use heavier suture material, particularly for large diameter vessels. One must remember that the tension in a vessel wall is proportional to the product of its radius and the pressure within, so it is much higher in the aorta than in the popliteal artery although the blood pressure is almost identical. Silk sutures had been used in the original operation performed on our patient and had parted.

It seems that failure of the arterial wall itself, although believed to be of importance by some authors (Stoney et al., 1965), is a relatively uncommon cause of aneurysm, and aneurysm is rare following endarterectomy compared with its incidence after prosthetic replacement.

In conclusion the current available literature would suggest that the type and strength of suture used and the strict avoidance of sepsis are the most important factors in avoiding this complication of reconstructive arterial surgery.

Acknowledgements

We wish to thank the Medical Artists and Photographic Departments of Hammersmith Hospital and Royal Postgraduate Medical School for the illustrations and also Miss Pauline Tarbard for typing the manuscript.

References

COOLEY D. A. and DEBAKEY M. E. (1952) Surgical consideration of intrathoracic aneurysms of aorta and great vessels. *Ann. Surg.* **135**, 660–680.

CUTLER E. C. and DUNPHY J. E. (1941) The use of silk in infected wounds. *New Engl. J. Med.* **224**, 101–107.

DEBAKEY M. E., CRAWFORD E. S., COOLEY D. A. and MORRIS G. C. J. R. (1958) Surgical considerations of occlusive disease of the abdominal aorta and iliac and femoral arteries. Analysis of 803 cases. *Ann. Surg.* **148**, 306–324.

EASTCOTT H. H. G. (1973) *Arterial Surgery.* London, Pitman, p. 293.

MARTIN P. C. G. (1963) *Indications and Techniques in Arterial Surgery.* Edinburgh, Livingstone, p. 86.

MOORE W. S. and HALL A. D. (1970) Late suture failure in the pathogenesis of anastomotic false aneurysms. *Ann. Surg.* **172**, 1064–1068.

SAWYERS J. L., JACOBS J. K. and SUTTON J. P. (1967) Peripheral anastomotic aneurysms development following reconstruction with prosthetic grafts. *Arch. Surg.* **95**, 802–809.

SHATZ I. J., FAIRBURN J. F. and JUERGENS J. L. (1962) Abdominal aortic aneurysms: a reappraisal. *Circulation* **26**, 200–205.

SHEIL A. G. R., REEVE T. S., LITTLE J. M., COUPLAND G. A. E. and LOEWENSHAL J. (1969) Aorto-intestinal fistulas following operations upon the abdominal aorta and iliac arteries. *Br. J. Surg.* **56**, 840–843.

SPRATT E. M., DORAN M. L. and BAIRD R. J. (1967) False aneurysms in the lower extremity. *Surg. Gynecol. Obstet.* **124**, 562–566.

STONEY R. J., ALBO R. J. and WYLIE J. (1965) False aneurysms occurring after arterial grafting operations. *Am. J. Surg.* **110**, 153–161.

SWAN H., MAASKI C., JOHNSON M. and GROVER R. (1950) Arterial homografts. Resection of thoracic aortic aneurysm using a stored human arterial transplant. *Arch. Surg.* **61**, 732–737.

VOORHEES A. B. J. R., JARETZLA A. and BLAKEMORE A. H. (1952) The use of tubes constructed from vinyl cloth in bridging arterial defects. *Ann. Surg.* **135**, 332–336.

Br. J. Surg. Vol. 62 (1975) 737–740

Gastric acid secretion following renal transplantation

S. F. CANAVAN, J. D. BRIGGS AND P. R. F. BELL*

SUMMARY

Gastric acid secretion studies were performed in 10 patients on regular dialysis and again following transplantation. While on dialysis, the acid output was high, with mean peak values after pentagastrin of 37·2 mEq/h in males and 26·3 mEq/h in females. These compared with values in normal subjects of 21·6 mEq/h in males and 12·3 mEq/h in females.

Following transplantation continuous steroid therapy was given. Repeat gastric acid secretion studies showed no significant change, with values of 37·1 mEq/h in males and 24·6 mEq/h in females. The high incidence of gastro-intestinal haemorrhage and perforation following transplantation is probably due mainly to steroid therapy, but the ulcerogenic effect of steroids would not seem to be mediated by increased gastric acid secretion.

Introduction

This study was prompted by the high incidence of peptic ulceration following renal transplant surgery. Duodenal ulceration or multiple gastric erosions associated with a high mortality are particularly common (Penn et al., 1968; Moore and Hulme, 1969; Hadjiyannakis et al., 1971).

We have investigated the possibility that these patients are prone to peptic ulcer disease following transplantation because of hypersecretion of gastric acid. The basis for this rests on two facts: first, that steroids are known to increase the parietal cell mass with an increase in acid secretion in experimental animals (Clarke et al., 1960; Cooke and Grossman, 1966), and secondly, that patients on regular dialysis therapy have been shown to have a high acid output (Gordon et al., 1972; Ventkateswaran et al., 1972; Shepherd et al., 1973) and are prone to develop peptic ulceration (McLeod et al., 1966; Pendras and Erickson, 1966; Goldstein et al., 1967; Ventkateswaran et al., 1972; Shepherd et al., 1973).

It is possible that steroid therapy might further increase acid secretion and the susceptibility to peptic ulceration. Hence the present study was undertaken to examine the effect of immunosuppressive therapy on gastric acid secretion after transplantation.

Patients and methods

Between May 1969 and December 1973, 79 renal transplants were carried out in a total of 71 patients. There were 42 males and 29 females with a mean age of 36 years (range 16–47 years). Five of the kidneys were obtained from living donors, and the remaining 74 from cadavers. Before transplantation all the patients were maintained on twice- or thrice-weekly haemodialysis with a total of 20–24 hours per week.

Following transplantation prednisolone was given in a decreasing dose of 200 mg on day 1 to 40 mg on day 17, with a slower reduction thereafter to 15 mg at 3 months. Prednisolone 1 g was given intravenously at the time of transplantation and was repeated up to a maximum of 6–8 g during rejection episodes. Azathioprine was given as a single daily dose which ranged from 25 to 200 mg. The dose was adjusted to maintain the total white blood cell count between 5000 and 8000/mm^3. All the patients were given aluminium hydroxide (Aludrox) in a dosage of 30 ml 4-hourly for the first month after transplantation. Thereafter Aludrox was usually only taken as required for the relief of dyspepsia.

While on haemodialysis 10 patients (5 males and 5 females) were selected at random for gastric acid studies. Eight of these 10 patients also had barium meals performed (4 before and 4 after transplantation), and all were questioned for dyspeptic symptoms. The gastric acid studies were repeated, usually at about 3 months after transplantation. Nine of the 10 patients had functioning kidneys at this time.

The technique used was that of Johnston and Jepson (1967), and normal values for comparison were taken from the work of Baron (1963). Following an overnight fast a nasogastric tube was passed and residual gastric contents aspirated. Thereafter a collection of basal gastric secretion was obtained for the next two 15-minute periods. After the basal collection, pentagastrin 6 μg/kg body weight was given by intramuscular injection. Gastric juice was then aspirated for the next four 15-minute periods. Continuous mechanical aspiration was used throughout, augmented by manual aspiration and/or repositioning of the tube if drainage was not satisfactory and continuous at any time. The acid output was calculated after titration of an aliquot to neutrality with N10 sodium hydroxide using phenol red as an indicator. The peak output was defined as twice the maximum value of acid output during any two consecutive 15-minute periods.

Results

Details of the 10 patients who had gastric acid secretion studies are given in *Table I.* These patients were representative of the whole group in terms of age and sex. Barium meal studies showed a duodenal ulcer in only 1 of the 8 patients examined. Four of the

---

*Renal Unit and University Department of Surgery, Western Infirmary, Glasgow.

Requests for reprints to J. D. Briggs, Renal Unit, Western Infirmary, Glasgow G11 6NT.

Present address of P. R. F. Bell: Department of Surgery, University of Leicester.

10 patients had dyspepsia before transplantation and a further patient developed dyspepsia following his transplant. *Table II* shows the results of the gastric acid secretion studies with normal values for comparison and significance levels.

In males the mean basal acid output was 3·8 mEq/h before and 3·4 mEq/h after transplantation. Both values were significantly greater than those in normal subjects. In females the corresponding figures were 1·2 mEq/h and 1·4 mEq/h, and they did not differ significantly from those in normal subjects. In the pre-transplant studies, the mean peak acid output following pentagastrin was 37·2 mEq/h in males and 26·3 mEq/h in females. Following transplantation there was no significant change in peak acid output, the mean values being 37·1 mEq/h in males and 24·6 mEq/h in females. Maximal acid concentration was slightly higher both in males (116 mEq/l) and females (104 mEq/l) while on regular dialysis than in normal subjects and did not change significantly after transplantation (males 122 mEq/l, females 94 mEq/l).

Five of the 71 patients had an episode of gastrointestinal bleeding due to peptic ulceration and one had a perforation. Four of those who bled and the patient whose ulcer perforated recovered following surgery but the remaining one died of uncontrollable bleeding. The incidence of haemorrhage from peptic ulcer was 7 per cent. Unfortunately, none of these patients was amongst those selected at random for acid secretion studies.

Discussion

Haemorrhage and perforation due to peptic ulceration are two of the more dangerous complications of renal transplantation and carry a high mortality. The combined incidence of these complications was found by

Table I: CLINICAL DETAILS OF THE 10 PATIENTS UNDERGOING GASTRIC ACID STUDIES

Patients	Age	Diagnosis	Duration of dialysis (mth)	Interval between first test and transplantation (mth)	Interval between transplantation and second test (mth)	Prednisolone dose at time of second test (mg/d)
Males						
D. F.	42	GN	38	1	3	25
A. T.	30	CPN	11	2	3	20
G. W.	45	ATN	28	11	1	15
H. C.	20	GN	17	11	21	40
R. P.	38	CPN	25	9	14	15
Females						
M. H.	22	GN	10	1	3	20
H. H.	40	GN	32	9	3	30/0*
M. C.	42	CPN	27	11	3	15
C. S.	37	GN	16	6	4	25
C. D.	20	CPN	4	4 d	2 w	40

GN, Glomerulonephritis. CPN, Chronic pyelonephritis. ATN, Persisting acute tubular necrosis.
* 30 mg on alternate days.

TABLE II: RESULTS OF GASTRIC ACID SECRETION STUDIES

	Before transplantation			After transplantation		
Patients	Basal acid output (mEq/h)	Peak acid output (mEq/h)	Maximal acid concentration (mEq/l)	Basal acid output (mEq/h)	Peak acid output (mEq/h)	Maximal acid concentration (mEq/l)
Males						
D. F.	4·2	28·8	90	3·2	31·8	110
A. T.	4·8	31·8	130	4·2	36·0	118
G. W.	0·0	44·8	116	0·0	48·0	140
H. C.	4·8	37·6	108	4·2	35·6	120
R. P.	5·2	43·4	134	5·4	34·0	120
Mean±s.d.	3·8±2·2	37·2±6·9	115·6±17·7	3·4±2·1	37·1±6·3	121·6±11·1
Normal males						
Mean±s.d.	1·3±1·6	21·6±13·8	94·7±35·1	1·3±1·6	21·6±13·8	94·7±35·1
*P**	<0·01	<0·05	NS	<0·05	<0·05	NS
Females						
M. H.	0	16·0	102	0·8	24·6	110
H. H.	0	18·0	100	0·6	13·0	114
M. C.	0	25·4	99	1·2	24·0	70
C. S.	2·2	35·4	122	3·2	33·2	110
C. D.	4·0	36·6	96	1·4	28·0	78
Mean±s.d.	1·2±1·8	26·3±9·5	103·8±10·4	1·4±1·0	24·6±7·4	94·4±19·5
Normal females						
Mean±s.d.	1·1±1·8	12·3±9·0	87·2±37·8	1·1±1·8	12·3±9·0	87·2±37·8
*P**	NS	<0·005	NS	NS	<0·01	NS

* Significance levels using Student's *t*-test; comparison of patients with normal subjects.
NS, Not significant.

Penn et al. (1968) to be 5 per cent and by Hadjiyannakis et al. (1971) to be 11 per cent, with a mortality rate of 50 and 60 per cent respectively.

Although debate continues as to the cause of duodenal ulceration, there is general agreement that increased gastric acid secretion plays some part. Most previous reports have shown increased acid secretion in patients on regular haemodialysis (Gordon et al., 1972; Ventkateswaran et al., 1972; Shepherd et al., 1973), with higher than normal values following pentagastrin administration (Ventkateswaran et al., 1972; Shepherd et al., 1973), although Gordon et al. (1972) could confirm this only for female dialysis patients. In the present study basal acid output was high in males while on regular dialysis, but in both sexes the administration of pentagastrin produced high peak acid outputs. These findings are similar to those of Ventkateswaran et al. (1972) and Shepherd et al. (1973). It is of interest that in non-dialysed patients with chronic renal failure a similar incidence of hypersecretion has not been found (Ventkateswaran et al., 1972). In addition to these findings of high gastric acid secretion, there are numerous reports of an increase in the incidence of peptic ulceration in regular dialysis patients (McLeod et al., 1966; Pendras and Erickson, 1966; Goldstein et al., 1967; Ventkateswaran et al., 1972; Shepherd et al., 1973). Thus, patients presenting for transplantation are already a high-risk group.

It is widely believed that the very high incidence of peptic ulceration following transplantation is due mainly to steroid therapy. The results of this study have shown that no further increase in acid output occurs following transplantation in spite of a high intake of steroids. This suggests that steroids may not exert their ulcerogenic effect through the medium of increased acid secretion. Only one of the patients tested developed peptic ulceration but 3 patients had dyspepsia. In addition, none of the patients who suffered from bleeding or perforation had acid secretion studies performed, mainly because these complications occurred early in their postoperative course.

Other ways in which steroid therapy may contribute to the problem of peptic ulcer are by masking symptoms and signs (Beck et al., 1950; Sautter and Ziffren, 1959), causing deterioration in connective tissue (Creditor et al., 1950), and decreasing the production of gastric mucus (Menguy and Masters, 1963; Desbaillets and Menguy, 1967). Other factors which could contribute to peptic ulceration in the transplanted patient are stress, both physical and emotional, and hyperparathyroidism with hypercalcaemia (Barreras and Donaldson, 1967). Hypercalcaemia does not, however, occur commonly enough to be an important factor.

In view of the high mortality from peptic ulcer complications following transplantation, prophylaxis and effective treatment are important. Antacid therapy can be used in an attempt to prevent ulcer formation, but this practice is not without its drawbacks. Phosphate binding gels may cause hypophosphataemia and osteomalacia (Lotz et al., 1968). Magnesium intoxication can occur if magnesium salts are given to the patient with poor renal function (Hirschfelder, 1934; Alfrey et al., 1970), and hypercalcaemia may follow the use of calcium salts (Stiel et al., 1967; Malone and Horn, 1971). In addition, unless antacids are used almost continuously, they cannot produce an effective and lasting reduction in gastric acidity. As combined steroid and antacid therapy may mask symptoms and thus delay recognition of the presence of peptic ulceration, a more rational approach might be to give antacids only if dyspepsia develops.

More important than antacid therapy is the recognition and treatment of peptic ulcer, if this is present, prior to transplantation. It is now the policy in our unit to carry out barium meal examinations routinely and in some cases gastroscopy as well in potential transplant patients. If a duodenal ulcer is present, elective pyloroplasty and vagotomy are carried out before transplantation. Routine barium meals are performed following transplantation. Only by earlier recognition of the presence of peptic ulcer will the high morbidity rate resulting from its complications be reduced.

References

ALFREY A. C., TERMAN D. S., BRETTSCHNEIDER L., SIMPSON K. M. and OGDEN D. A. (1970) Hypermagnesemia after renal transplantation. *Ann. Intern. Med.* **73**, 367–371.

BARON J. H. (1963) Studies of basal and peak acid output with an augmented histamine test. *Gut* **4**, 136–144.

BARRERAS R. F. and DONALDSON R. M. (1967) Role of calcium in gastric hypersecretion. *New Engl. J. Med.* **276**, 1122–1124.

BECK J. C., BROWNE J. S. L., JOHNSON L. G., KENNEDY B. J. and MACKENZIE D. W. (1950) Occurrence of peritonitis during A.C.T.H. administration. *Can. Med. Assoc. J.* **62**, 423–426.

CLARKE S. D., NEILL D. W. and WELBOURN R. B. (1960) The effects of corticotrophin and corticoids on secretion from denervated gastric pouches in dogs. *Gut* **1**, 36–43.

COOKE A. R. and GROSSMAN M. I. (1966) Effect of hydrocortisone on secretion of acid and pepsin by Heidenhain pouches. *Proc. Soc. Exp. Biol. Med.* **123**, 704–710.

CREDITOR M. C., BEVANS M., MUNDY W. L. and RAGAN C. (1950) Effect of A.C.T.H. on wound healing in humans. *Proc. Soc. Exp. Biol. Med.* **74**, 245–247.

DESBAILLETS L. and MENGUY R. (1967) Inhibition of gastric mucous secretion by A.C.T.H. An experimental study. *Am. J. Dig. Dis.* **12**, 582–588.

GOLDSTEIN H., MURPHY D., SOKOL A. and RUBINI M. E. (1967) Gastric acid secretion in patients undergoing chronic dialysis. *Arch. Intern. Med.* **120**, 645–653.

GORDON E. M., JOHNSON A. G. and WILLIAMS G. (1972) Gastric assessment of prospective renal transplant patients. *Lancet* **1**, 226–229.

HADJIYANNAKIS E. J., EVANS D. E., SMELLIE W. A. B. and CALNE R. Y. (1971) Gastrointestinal complications after renal transplantation. *Lancet* **2**, 781–785.

HIRSCHFELDER A. D. (1934) Clinical manifestations of high and low plasma magnesium. Dangers of Epsom salt purgation in nephritis. *JAMA* **102**, 1138–1141.

JOHNSTON D. and JEPSON K. (1967) Use of pentagastrin as test of gastric acid secretion. *Lancet* **2**, 585–588.

LOTZ M., ZISMAN E. and BARTTER F. C. (1968) Evidence for a phosphorus-depletion syndrome in man. *New Engl. J. Med.* **278**, 409–415.

MCLEOD L. E., MANDIN H., DAVIDMAN M., ULNAN R. and LAKEY W. H. (1966) Intermittent haemodialysis in terminal chronic renal failure. *Can. Med. Assoc. J.* **94**, 318–327.

MALONE D. N. S. and HORN D. B. (1971) Acute hypercalcaemia and renal failure after antacid therapy. *Br. Med. J.* **1**, 709–713.

MENGUY R. and MASTERS Y. F. (1963) Effect of cortisone on mucoprotein secretion by gastric antrum of dogs: pathogenesis of steroid ulcer. *Surgery* **54**, 19–28.

MOORE T. C. and HULME D. M. (1969) The period and nature of hazard in clinical renal transplantation: the hazard to patient survival. *Ann. Surg.* **168**, 865–870.

PENDRAS J. P. and ERICKSON R. V. (1966) Haemodialysis: a successful therapy for chronic uraemia. *Ann. Intern. Med.* **64**, 293–311.

PENN I., GROTH C. G., BRETTSCHNEIDER L., MARTIN A. J., MARCHIORO T. L. and STARZL T. E. (1968) Surgically correctable intra-abdominal complications before and after renal homotransplantation. *Ann. Surg.* **168**, 865–870.

SAUTTER R. D. and ZIFFREN S. E. (1959) Adrenocortical steroid therapy resulting in unusual gastrointestinal complications. *Arch. Surg.* **79**, 346–356.

SHEPHERD A. M. M., STEWART W. K. and WORMSLEY K. G. (1973) Peptic ulceration in chronic renal failure. *Lancet* **1**, 1357–1359.

STIEL J. N., MITCHELL C. A., RATCLIFFE F. J. and PIPER D. W. (1967) Hypercalcaemia in patients with peptic ulceration receiving large doses of calcium carbonate. *Gastroenterology* **53**, 900–904.

VENTKATESWARAN P. S., JEFFERS A. and HOCKEN A. G. (1972) Gastric acid secretion in chronic renal failure. *Br. Med. J.* **4**, 22–23.

Br. J. Surg. Vol. 62 (1975) 741–744

Collagen biosynthesis in normal and hypertrophic scars and keloid as a function of the duration of the scar

R. D. PETER CRAIG, J. DAVID SCHOFIELD AND DAVID S. JACKSON*

SUMMARY

The rates of collagen biosynthesis and the tissue concentrations of collagen in normal scar, hypertrophic scar and keloid were determined as a function of the duration of the lesions. The rate of collagen synthesis in normal scar was approximately constant between 6 months and 20 years after the initial wounding, but in both hypertrophic scar and keloid the rate was initially approximately twice that in normal scar, and 2–3 years after wounding it fell to approximately the same level as in normal scar. The tissue concentration of collagen appeared to be relatively constant in normal scar with respect to the time elapsed after wounding, but in both types of abnormal scar it was initially somewhat lower than normal scar and then rose to values higher than in normal scar after about 2–3 years. Since similar results were obtained for both types of abnormal scar in terms of the rates of collagen biosynthesis with respect to the time elapsed after wounding and also in terms of the tissue concentrations of collagen, this may indicate that the events in the pathogenesis of both abnormal scar types are similar. The results also raise the possibility that the formation of both types of abnormal scar may occur in two phases: an initial phase characterized by abnormally high rates of collagen biosynthesis, and a later phase characterized by essentially normal rates of collagen biosynthesis.

RECENT studies have indicated that the excessive accumulation of collagen seen in hypertrophic scar and keloid may, at least in part, be due to abnormally high rates of synthesis of this protein compared with normal scar (Cohen et al., 1971; Fleckman et al., 1973; Craig et al., 1975). Determination of the activity of the enzyme collagen proline hydroxylase, which catalyses the conversion of peptide-bound proline to hydroxyproline during collagen biosynthesis, and the activity of which is often regarded as an index of the rate of collagen synthesis, has shown that it is markedly elevated in both abnormal scar types, suggesting increased rates of synthesis (Cohen et al., 1971; Fleckman et al., 1973). We have measured the rate of collagen synthesis in normal and abnormal scars using the method described by Uitto (1970), in which the incorporation of radioactivity into non-diffusible peptide-bound hydroxyproline by tissue minces incubated with [^{14}C]-proline *in vitro* is determined. In agreement with the conclusions from measurement of the activity of proline hydroxylase, we observed that the rate of collagen biosynthesis, as measured by Uitto's technique, was significantly elevated in both abnormal scar types compared with that in normal scar (Craig et al., 1975), although we did not observe such dramatic increases in hydroxyproline synthesis as were observed for the increases in proline hydroxylase activity in the abnormal scar types.

In the present study we have again made use of the technique described by Uitto (1970) to determine the rates of synthesis of collagen in normal and hypertrophic scar and keloid with respect to the time elapsed after the initial wounding. We have also determined the tissue concentrations of collagen in the different scar types as a function of duration of the wound. Our results again indicate that the abnormal scars are biochemically different compared with normal scars, but the events occurring during the development of both hypertrophic scar and keloid appear to be similar and these observations may indicate that these two lesions are manifestations of the same basic defect, as discussed previously by Peacock et al. (1970).

Materials and methods

Determination of the rate of collagen biosynthesis

The rate of collagen biosynthesis in normal scar, hypertrophic scar and keloid was determined by measuring the rate of incorporation of radioactivity into non-dialysable hydroxyproline by excised tissues incubated *in vitro* with L-[^{14}C]-proline, according to the method of Uitto (1970). Hydroxyproline is found almost exclusively in collagen, constituting about 14 per cent of the dry weight of the protein, and the amounts of this imino acid are relatively constant in collagens from various tissues in humans (Eastoe, 1967; Schofield et al., 1971). The rate of hydroxyproline formation is therefore considered to be a good indication of the rate of collagen biosynthesis. Also, hydroxyproline is not directly incorporated into collagen polypeptides but rather arises through enzymic hydroxylation of certain proline residues after their incorporation into the growing polypeptide chains, and hence the radio-labelled precursor with which one incubates the tissues is proline rather than hydroxyproline.

Scar tissue was obtained during surgery and was transferred quickly to the laboratory in ice cold normal saline. Subcutaneous fat and epidermis were trimmed off and the remaining tissue was minced finely with scissors to approximately 0·5-mm diameter

---

* Plastic Surgery Unit, University Hospital of South Manchester, and Department of Medical Biochemistry, University of Manchester.

Present address of J. D. Schofield: University of Manchester, Geigy Unit for Research into Aging, Department of Geriatric Medicine, University Hospital of South Manchester.

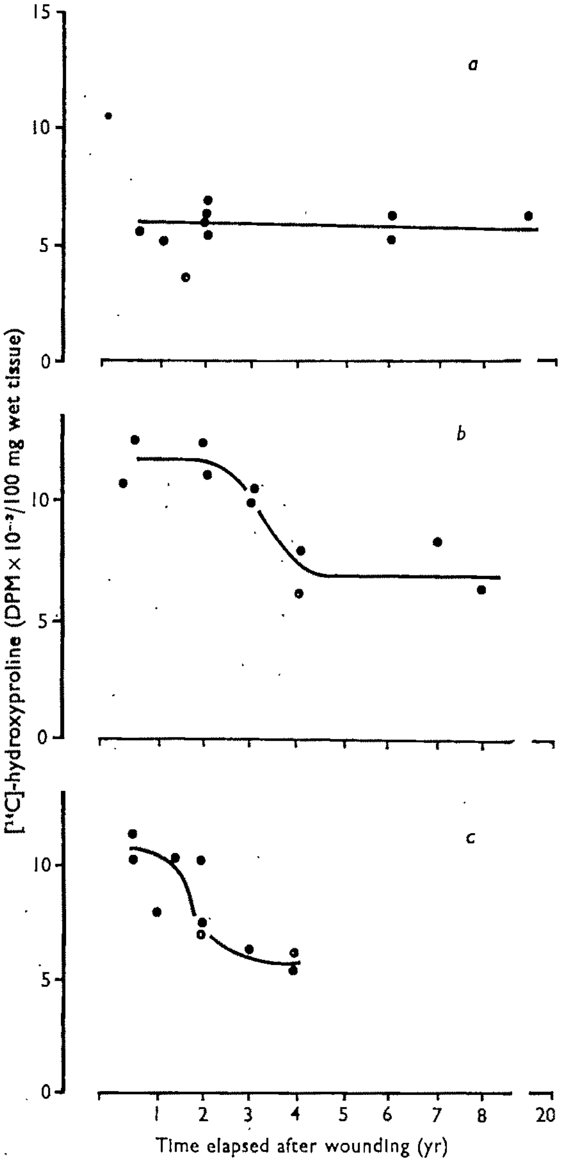


Fig. 1. Collagen synthesis with respect to the duration of various types of scar. *a*, Normal; *b*, hypertrophic; *c*, keloid.

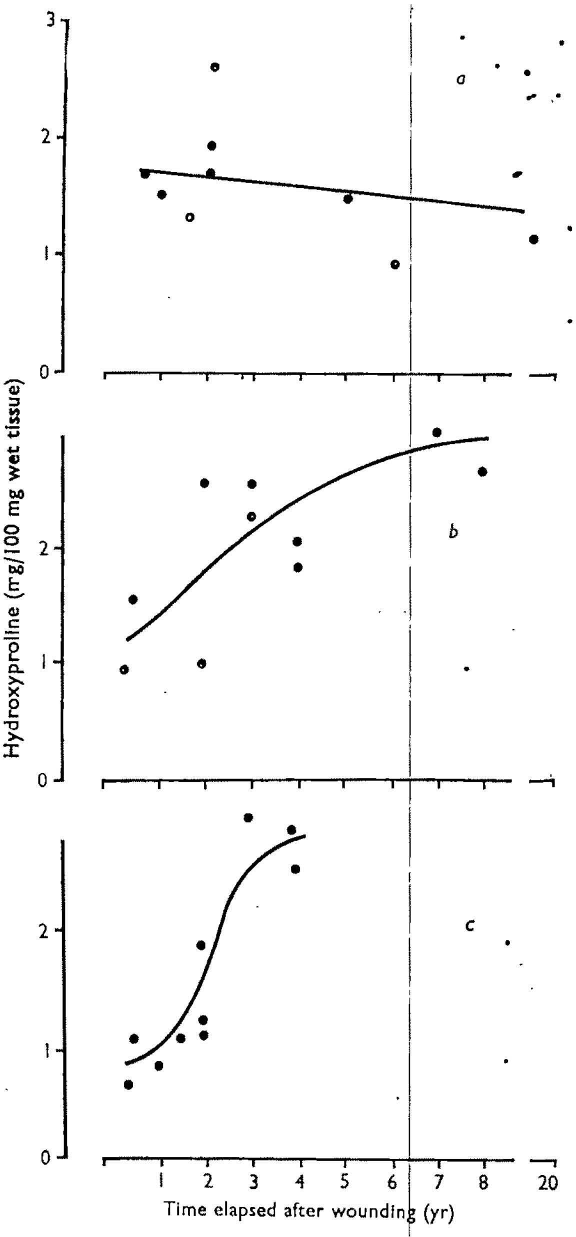


Fig. 2. Collagen concentration with respect to the duration of various types of scar. *a*, Normal; *b*, hypertrophic; *c*, keloid.

pieces. Aliquots of the minced tissues (100 mg wet weight) were then incubated with L-[^{14}C]-proline for 18 hours and the radioactivity incorporated into non-diffusible peptide-bound hydroxyproline was determined as described previously (Uitto, 1970; Craig et al., 1975).

Determination of tissue concentration of collagen

The tissue concentration of collagen in the different scars was determined again by making use of the fact that hydroxyproline occurs almost exclusively in this protein. Aliquots of tissue were hydrolysed in 6 M-HCl and the hydroxyproline in the hydrolysates was determined according to the method of Stegemann and Stalder (1967).

Results

Collagen biosynthesis in normal and hypertrophic scars and keloid in relation to time elapsed after wounding

Our previous results (Craig et al., 1975) indicated that incorporation of radioactivity into hydroxyproline is linear for up to 18 hours using Uitto's (1970) technique, and that the body site from which scar tissue was taken had relatively little influence on the rate of collagen synthesis. The tissues used in the present study were from a number of different sites and an incubation time of 18 hours was used throughout.

Although we previously observed that the rate of synthesis of collagen in both abnormal scar types was significantly elevated compared with normal scar (Craig et al., 1975), no regard was taken of the effect of the duration of the lesion on the rate of synthesis in that study. The results of determination of the rates of collagen synthesis as a function of the duration of the various types of lesion are presented in *Fig.* 1. Each point represents the mean value for the amount of label incorporated into non-diffusible peptide-bound hydroxyproline by replicate 100-mg aliquots (not less than 3) of tissue minces of the same scar sample, and each sample was derived from a different patient. The values for the individual aliquots from each scar sample were always found to be within ±10 per cent, or better, of the mean value. The regression lines in *Figs.* 1*a* and 2*a* were calculated by the method of least squares.

When collagen synthesis was examined in normal scar at different times after wounding it was found that the rate of synthesis was quite constant between 6 months and 20 years (*Fig.* 1*a*). The results with hypertrophic scar and keloid, however, contrasted markedly with those obtained with normal scar. In both types of abnormal scar the rate of collagen synthesis over the first 2–3 years was approximately twice as high as in normal scar (*Fig.* 1). After 2–3 years, however, the rate of collagen synthesis in both abnormal scar types fell to approximately the same level as in normal scar, that is to approximately 50 per cent of the early values.

Tissue concentration of collagen in normal and hypertrophic scars and keloid in relation to time elapsed after wounding

A comparison of the tissue concentrations of collagen in normal and hypertrophic scars and keloid was made by determining the amount of hydroxyproline present in acid hydrolysates of the tissue samples. These results indicated that the tissue concentration of collagen in normal scars (*Fig.* 2*a*) appeared to be relatively constant with respect to the time elapsed after wounding (approximately 1·5 mg hydroxyproline/100 mg wet tissue). In hypertrophic scar and keloid, however, the initial values were approximately 1·1 and 0·8 mg respectively, but they increased such that at 4 years after wounding the values for hypertrophic scar and keloid were approximately 2·3 and 2·7 mg respectively (*Fig.* 2*b*, *c*). Hence, both the rate of collagen synthesis and the tissue concentration of collagen were observed to vary considerably with respect to time elapsed after wounding in the abnormal scars, whereas in normal scar these parameters appeared to be relatively constant. Furthermore, the fall in the rate of synthesis in both hypertrophic scar and keloid from approximately the same high value to about the same approximately normal value, and the increase in the collagen content of the abnormal scars from approximately normal values to values significantly higher than normal, both occurred at about the same time, that is about 2–3 years after the initial wounding.

Discussion

Determination of the rates of collagen biosynthesis in normal scar, hypertrophic scar and keloid, either by measurement of the activity of the enzyme collagen proline hydroxylase (Cohen et al., 1971; Fleckman et al., 1973) or by measurement of the incorporation of radioactivity into hydroxyproline (Craig et al., 1975), have suggested that abnormally high rates of biosynthesis of collagen may be a contributory factor leading to the formation of the abnormal scars. Enzyme activity was approximately fourteen times higher in keloid, and was approximately four times higher in hypertrophic scar, when compared with normal scar (Cohen et al., 1971). Although we also observed an increased rate of collagen synthesis in the abnormal scars, as determined by measurement of the incorporation of radioactivity into hydroxyproline upon incubation of tissues with [^{14}C]-proline *in vitro*, the increases were somewhat less than twofold in both abnormal scar types compared with normal scar (Craig et al., 1975). However, these studies were undertaken without regard to the duration of the lesion.

In the present study the rate of collagen synthesis was examined with respect to the time elapsed after wounding (*Fig.* 1). Normal scar synthesized collagen at a relatively constant rate (*Fig.* 1*a*), but in both hypertrophic scar and keloid the rate of collagen synthesis during the first 2–3 years after wounding was approximately twice as high as in normal scar and subsequently fell to the level found in normal scar (*Fig.* 1*b*, *c*).

The tissue concentration of collagen in normal scar was relatively constant with respect to the time elapsed after wounding, whereas in both abnormal types of scar there appeared to be a continuous increase up to at least 4 years (*Fig.* 2). Such changes in the collagen content of keloid were not observed in a previous study (Harris and Sjoerdsma, 1966). However, the minimum period which elapsed between wounding and examination of the tissue was 2 years in that study, and it is possible that such changes that might occur had already done so in the 2 individuals examined at that time. It has been assumed in the present work and in that of Harris and Sjoerdsma (1966) that the hydroxyproline content of the collagen in each type of scar is the same. This seems to be a reasonable assumption in view of the constancy of the hydroxyproline contents of collagens from a wide variety of human tissues such as skin, tendon and bone (Eastoe, 1967; Schofield et al., 1971).

Peacock et al. (1970) have made the point that hypertrophic scar and keloid formation may be manifestations of the same basic defect, and it is interesting in this respect that in both abnormal scar types the pattern of the changes observed both in the rates of synthesis and in the tissue concentrations of collagen are very similar (*Figs.* 1, 2). These observations may indicate that the events leading to the pathogenesis of hypertrophic scars and keloids are essentially similar.

In normal scar it is apparent that the rates of synthesis and degradation of collagen are in equilibrium since there is no excessive accumulation of collagen in either case. Initially the rate of collagen synthesis in hypertrophic scar and keloid is twice as high as in normal scar (*Fig.* 1), but 2 or 3 years later falls to the same level as in normal scar. Despite this fall in rate of collagen synthesis there is a continued excessive deposition of collagen, which suggests that there is also deficiency in the mechanism of collagen degradation in the two abnormal tissues. Examination of the collagenase produced by explants of hypertrophic scar, keloid and normal skin (Milsom and Craig, 1973) revealed no significant differences either in the amount of the enzyme produced or in the nature of the enzyme compared with normal skin, although a comparison between the two abnormal scar types and normal scar was not made in that study. It is, however, possible, as suggested by Milsom and Craig (1973), that activation of procollagenase, the inactive zymogen of collagenase, is suppressed in the abnormal scars *in vivo*. This could occur either through the presence of a suppressor of the enzyme(s) which activate procollagenase or through the presence of a defective activator enzyme, and a recent report (Harper and Gross, 1974) has indicated that the activity of an activator of procollagenase is indeed low in keloid and hypertrophic scar. It would appear, therefore, that the degradation of collagen, as well as its biosynthesis, is defective in keloid and hypertrophic scar.

These observations raise the possibility that there may be two phases in the production of hypertrophic scar and keloid, the first being characterized by abnormally high rates of collagen synthesis and possibly abnormal degradation of collagen, and the second being characterized by essentially normal rates of collagen synthesis and presumably decreased degradation.

Acknowledgements

This work was supported by a grant from the Manchester Regional Hospital Board and through the provision of a post-doctoral fellowship to J. D. S. by Turner & Newall Ltd.

References

COHEN I. K., KEISER H. R. and SJOERDSMA A. (1971) Collagen synthesis in human keloid and hypertrophic scar. *Surg. Forum* **22**, 488–489.

CRAIG R. D. P., SCHOFIELD J. D. and JACKSON D. S. (1975) Collagen biosynthesis in normal human skin, normal and hypertrophic scar and keloid. *Eur. J. Clin. Invest.* **5**, 69–74.

EASTOE J. E. (1967) Composition of collagen and allied proteins. In: RAMACHANDRAN G. N. (ed.) *Treatise on Collagen*, Vol. 1. London, Academic Press, p. 1.

FLECKMAN P. H., JEFFREY J. J. and EISEN A. Z. (1973) A sensitive microassay for prolyl hydroxylase: activity in normal and psoriatic skin. *J. Invest. Dermatol.* **60**, 46–52.

HARPER E. and GROSS J. (1974) Collagenase and its zymogen. Protides of the biological fluids. 22nd Colloquium, Brugge, Belgium. Abstr. 114. Oxford, Pergamon, p. 92.

HARRIS E. D. and SJOERDSMA A. (1966) Collagen profiles in various clinical conditions. *Lancet* **2**, 707–711.

MILSOM J. P. and CRAIG R. D. P. (1973) Collagen degradation in cultured keloid and hypertrophic scar tissue. *Br. J. Dermatol.* **89**, 635–644:

PEACOCK E. E., MADDEN J. W. and TRIER W. C. (1970) Biological basis for the treatment of keloids and hypertrophic scars. *South. Med. J.* **63**, 755–760.

SCHOFIELD J. D., FREEMAN I. L. and JACKSON D. S. (1971) The isolation and amino acid and carbohydrate composition of insoluble collagens from various human tissues. *Biochem. J.* **124**, 467–473.

STEGEMANN H. and STALDER K. (1967) The determination of hydroxyproline. *Clin. Chim. Acta* **18**, 267–273.

UITTO J. (1970) A method for studying collagen biosynthesis in human skin biopsies *in vitro*. *Biochim. Biophys. Acta* **201**, 438–445.

Br. J. Surg. Vol. 62 (1975) 745–746

A technique for re-exploration of the saphenofemoral junction for recurrent varicose veins

ARTHUR K. C. LI*

SUMMARY

A safe and simple method is described for re-exploration of the saphenofemoral junction in patients with recurrent varicose veins following incomplete 'Trendelenburg operation'.

A MAJOR cause for recurrent varicose veins is inadequate groin dissection, with failure to ligate flush with the saphenofemoral junction (Hæger, 1967; Nabatoff, 1969; Lofgren and Lofgren, 1971). Re-exploration of this region is often beset with difficulties from previous scar tissue encasing the delicate dilated varices (Stein, 1967). A simple and expeditious method is described here which will overcome these dangers. This approach is familiar to vascular surgeons who use it in the exposure of the vessels at the groin for vein graft bypass operations.

Technique

The common femoral artery is first palpated and defined at the groin. The previous incision, if already correctly placed, may be used but it must be extended laterally over the femoral pulse (*Fig.* 1). The dissection begins at the lateral end of the incision, which is deepened through the fascia to expose the femoral artery within the femoral sheath. By incising the femoral sheath over the artery longitudinally for approximately 5 cm and then taking the dissection medially, the femoral vein can be readily displayed both above and below the saphenofemoral junction (*Fig.* 2). Since the previous operation will not have properly exposed the saphenofemoral junction and the femoral vein, the present plane of dissection will be deep to the scar tissue and therefore little difficulty is encountered.

Once the femoral vein and saphenofemoral junction have thus been exposed and the saphenous stump has been gently dissected from the surrounding tissues using a curved artery forceps such as a Fraser, an aneurysm needle with a silk ligature can be passed safely around the saphenofemoral junction, after which flush ligation with the femoral vein can be carried out (*Fig.* 3). The stump can be similarly ligated and the junction divided, thereby achieving control of the main source of retrograde incompetence.

The remaining dilated varices in the scar can be dealt with in two ways. A 'running stitch' through the scar tissue can be used to obliterate these plexuses of veins, or alternatively the scar tissue interlaced with the varices can be divided along the line of the previous incision between haemostatic clamps (*Fig.* 4). As the femoral vein is now well exposed, it is simple to check that no aberrant superficial veins join it distal to the saphenofemoral junction, and the deep external pudendal vein can be ligated.

Discussion

The majority of difficulties encountered in re-exploration of the saphenofemoral junction occur in patients in whom the previous incision had been correctly placed (Pratt, 1971) and attempts made to ligate the tributaries. It has been suggested that a higher incision should be made just below the inguinal ligament so that further dissection would be through normal tissue (Luke, 1954; Dodd and Cockett, 1956).

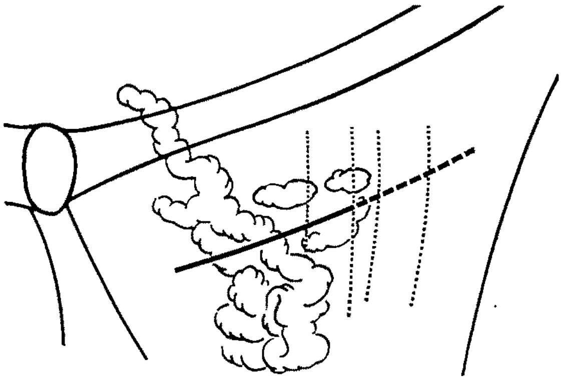


Fig. 1. The incision placed over the femoral pulse.

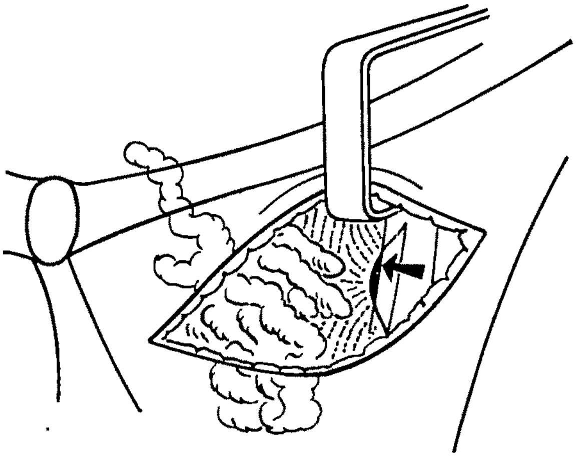


Fig. 2. Longitudinal exposure of the femoral artery in the femoral sheath.

---

* St Mary's Hospital, London.
Present address: Academic Department of Surgery, Royal Free Hospital, London.

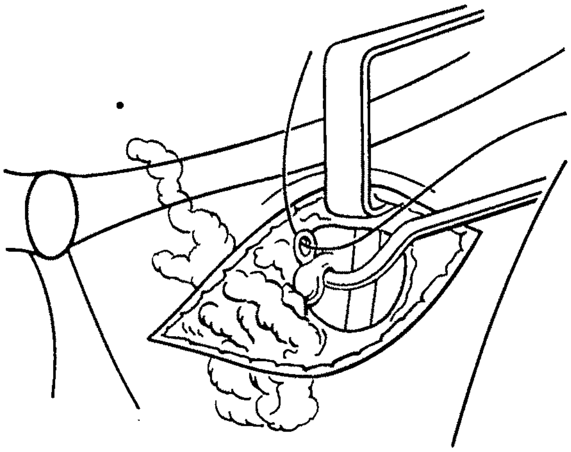


Fig. 3. Exposure of the saphenofemoral junction and flush ligation with the femoral vein.

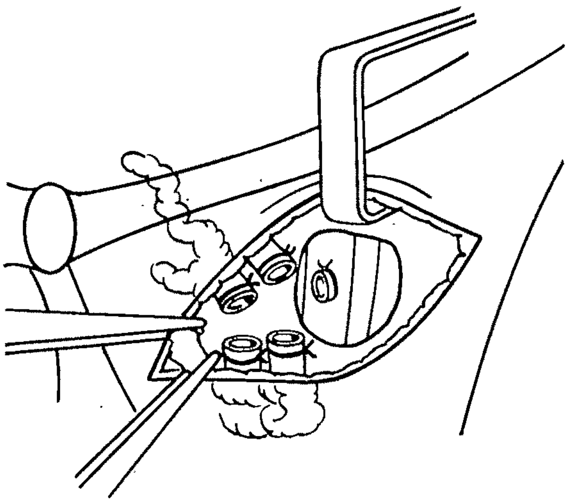


Fig. 4. Ligation of the tributaries.

However, when the previous incision is already high it may afford little room to manœuvre.

Emphasis has also been placed on seeking the femoral vein either from above the saphenofemoral junction (Dodd and Cockett, 1956) or from its medial aspect (Halliday, 1970). In the midst of scarred and adherent tissue it is far safer to dissect on to a pulsating artery than a compressible vein with all its ramifications of tributaries. Furthermore, early exposure of the femoral artery allows prompt control of the superficial external pudendal artery if necessary.

With previous techniques of re-exploration, troublesome bleeding may occur from the posterior aspect of an in-bulging varix situated further distal to the saphenofemoral junction. By the method suggested, early control of the femoral vein above and below that junction is obtained should it be necessary, and thus the haemorrhage can be contained.

In conclusion, the advantages of the technique described are threefold. First, there is a single incision instead of two. This is important as there is often an element of cosmetic complaint in patients with varicose veins. Secondly, the initial exposure is that of an artery which makes the operation simpler and safer and more expeditious than the hazardous exposure of a compressible vein in a small field. Lastly, the dissection is through normal tissue, thus avoiding the cicatrix with its enmeshed varices, and allows early control of the femoral vein above and below the saphenofemoral junction should it be necessary. This method of dealing with groin recurrences has been performed on more than 30 patients at St Mary's Hospital, London, and the results have been entirely safe and satisfactory.

Acknowledgement

I wish to thank Mr H. H. G. Eastcott for his encouragement and guidance in the preparation of this paper.

References

DODD H. and COCKETT F. B. (1956) *The Pathology and Surgery of Veins of the Lower Limb*. Livingstone, Edinburgh, pp. 278–279.

HÆGER K. (1967) 1084 Legs with recurrent varicose veins. An analysis after previous unsuccessful operations. *Zentralbl. Phlebol.* **6**, 12–20.

HALLIDAY P. (1970) Repeat high ligation. *Aust. NZ J. Surg.* **39**, 354–356.

LOFGREN E. P. and LOFGREN K. A. (1971) Recurrence of varicose veins after stripping operation. *Arch. Surg.* **102**, 111–114.

LUKE J. C. (1954) The management of recurrent varicose veins. *Surgery* **35**, 40–44.

NABATOFF R. A. (1969) Reasons for major recurrence following operations for varicose veins. *Surg. Gynecol. Obstet.* **128**, 275–278.

PRATT G. H. (1971) A technique for operation on the pathologic venous system. *Surg. Gynecol. Obstet.* **132**, 1076–1082.

STERN W. (1967) Dealing with difficulties and complications of varicose vein operations. *Med. J. Aust.* **1**, 554–556.

Br. J. Surg. Vol. 62 (1975) 747–749

Parathyroid identification by methylene blue infusion

DONALD L. GORDON, MOHAN C. AIRAN, WILLIAM THOMAS
AND LEON H. SEIDMAN*

SUMMARY

The intravenous infusion of methylene blue was investigated as a procedure that would identify parathyroid glands during operation in 17 patients with primary hyperparathyroidism. The dye was found to stain all adenomas, most hyperplastic glands and occasionally normal parathyroid glands. In addition, the frequency of glandular staining was directly related to the size of the gland, although size and histology may have been independent variables. Methylene blue infusion is a safe effective method of localizing abnormal parathyroid glands.

PARATHYROID gland localization is a perplexing problem to many surgeons. A meticulous exploration of the neck must be performed in primary hyperparathyroidism with every effort made to identify, by inspection and histological confirmation, all parathyroid tissue (Black and Haff, 1970). Detection is particularly difficult because of the small size of these glands, which are normally less than 7 mm in greatest diameter (Castleman, 1952). Atypical sites and variable numbers of parathyroid glands compound the surgeon's problem.

Clinical interest was attracted by the report of Klopper and Moe (1966) that intravenous infusion of toluidine blue distinctly stained the normal parathyroid glands of dogs. This was confirmed by Hurvitz et al. (1967), and the technique was successfully extended to humans in a subsequent report (Hurvitz et al., 1968). However, arrhythmias and cardiac arrest attributable to the dye eventually resulted in a decrease in its use (Pridgin et al., 1969; Yeager and Krementz, 1969; Singleton and Allums, 1970). An alternative was reported by Dudley (1971), who described parathyroid staining without complications in 17 patients after methylene blue infusion.

Methylene blue was infused by us in patients operated upon for primary hyperparathyroidism in an attempt to correlate the ability of the parathyroid gland to stain blue with its size and histology.

Patients and methods

Methylene blue was infused during neck exploration in 17 consecutive patients with primary hyperparathyroidism. Patients who had had previous operations on the neck were excluded from the study. A dose of 5 mg/kg body weight (230–500 mg) of a 1 per cent solution of methylene blue was prepared on the morning of operation in 500 ml of 0·9-N saline. The infusion, which lasted 45–60 minutes (average 50 minutes), was timed to end 15 minutes before completion of the dissection to the plane of the pretracheal fascia.

Each parathyroid gland was measured *in situ* after complete dissection but before biopsy. Note was made of the colour of the gland. When it was uncertain that a trace of dye was actually present it was considered to be absent. An attempt was made to biopsy all parathyroid glands. Most patients had all or parts equivalent to 3 parathyroid glands removed for therapy of primary hyperparathyroidism. Any extraparathyroid tissue that stained blue for longer than 45 minutes after the end of the infusion was biopsied.

Blood pressure, pulse, respiratory rate and ECG were monitored before, during and after the operation. Serum calcium levels were measured before operation and usually at daily intervals afterwards to assess the completeness of the operation.

Results

Primary hyperparathyroidism was confirmed in all the patients by tissue diagnosis and relief of hypercalcaemia within 48 hours of parathyroidectomy (Gordon et al., 1972). The final pathological diagnosis was a single parathyroid adenoma and hyperplasia in 11 patients, multiple parathyroid adenomas and hyperplasia in 2 patients, single adenoma in 1 patient and diffuse hyperplasia in 3 patients.

Sixty parathyroid glands were identified histologically while 3 additional glands were isolated but not biopsied. The staining affinity for the dye was directly related to the size of the parathyroid gland (*Table I*). Forty of the 46 (87 per cent) enlarged parathyroid glands were significantly discoloured by the dye, while only 3 of 12 (25 per cent) normal sized glands were stained. When this characteristic was correlated with the histological diagnosis, disregarding size, 16 out of 16 (100 per cent) adenomas stained, 23 out of 27 (85 per cent) hyperplastic glands stained and only 4 out of 15 (27 per cent) histologically normal glands stained blue (*Table II*). Parathyroid adenomas and enlarged hyperplastic parathyroid glands readily concentrated the dye, usually developing a dark blue colour. A less consistent colour of either a lighter blue or a violet tinge was noted in hyperplastic glands of normal size, enlarged glands that were histologically normal and glands whose size and histology were both normal. In 1 patient with an adenoma, 2 additional hyperplastic parathyroid glands were biopsied, but the staining characteristics were not noted in the record; therefore they could not be

---

* Department of Medicine, Surgery and Pathology, Mount Sinai Hospital Medical Center, Chicago, Illinois.

Requests for reprints to Donald L. Gordon, Director, Division of Endocrinology and Metabolism, Mount Sinai Hospital Medical [Center, 2755 West 15th Street, Chicago, Illinois 60608.

Table I: CORRELATION BETWEEN SIZE AND METHYLENE BLUE STAINING OF PARATHYROID GLANDS IN 17 PATIENTS

Size of gland (cm)	Staining characteristics (no. of glands)*	
	Stained	Unstained
>1·6	14	1
1·2–1·6	12	0
0·7–1·1	14	5
<0·7	3	9

* Staining characteristics are unknown for 2 hyperplastic glands. Three unstained, normal sized glands were not biopsied. The remaining 5 glands were not found or were not present.

Table II: CORRELATION BETWEEN HISTOLOGICAL DIAGNOSIS AND METHYLENE BLUE STAINING OF PARATHYROID GLANDS IN 17 PATIENTS

Histological diagnosis	Staining characteristics (no. of glands)	
	Stained	Unstained
Adenoma	16	0
Hyperplasia	23	4
Normal	4	11

included in the tabulations. Three additional normal sized, unstained parathyroid glands were noted but not biopsied. For this study these glands were not counted as parathyroids and are considered not to have been located. Assuming an average of 4 parathyroid glands per patient, 60 out of 68 (88 per cent) of the glands were proved by biopsy to be present. Ten parathyroid glands were not included in the tabulations due to lack of biopsy confirmation or documentation of staining characteristics or their not being found. This represented the experience in only 4 patients; the other 13 patients had all 4 glands located, the staining characteristics had been noted and they were biopsied.

There were 9 instances of non-parathyroid tissue staining blue for prolonged periods. These included two lymph nodes, the nodularity and/or cyst formation in 6 colloid goitres and the whole thyroid gland in 1 case of lymphocytic thyroiditis. No complications were noted during or following the operation that could be attributed to methylene blue.

Discussion

The diagnosis of primary hyperparathyroidism has continued to be made in most cases on the basis of persistent hypercalcaemia after exclusion of all other causes of this abnormality. However, a change in the surgical approach has gradually occurred. This evolved as a result of observations upon patients with persistent hypercalcaemia following removal of what was thought to be a solitary parathyroid adenoma. At re-exploration considerable variability in the size of the histologically abnormal glands was noted. In addition, as multiple glands were biopsied more routinely during the initial operation, a changing incidence of parathyroid hyperplasia with or without adenoma was diagnosed more frequently (Reinhoff et al., 1968; Straus and Paloyan, 1969; Egdahl, 1970; Haff et al., 1970). This had made it more imperative for accurate parathyroid localization techniques to be developed.

Preoperative localization of abnormal parathyroid glands has been reported using selenomethionine-75 scanning (DiGiulio and Morales, 1969), arteriography (Doppman et al., 1969) and venography with parathormone sampling of the venous effluent (Aurbach et al., 1973). Of these procedures, only angiography followed by selective venous parathormone sampling is able to distinguish between adenoma and hyperplasia. Yet even these procedures do not allow precise localization of adenomas (Aurbach et al., 1973; Shimkin and Powell, 1973). The ideal method should result in visualization of all the parathyroid glands, or at the very least all the abnormal glands. It should be both safe and readily available for use at large centres as well as smaller institutions. Intravenous infusion of methylene blue meets these criteria.

Parathyroid staining by methylene blue occurred in 42 out of 58 (76 per cent) histologically proved, parathyroid glands. This probably represents a modest overestimate of the gross staining capabilities of the dye. Three of the remaining glands were found unstained but not histologically confirmed as parathyroid tissue, while 5 other glands were not located. In view of the fall of serum calcium to normal levels in these patients, the glands that were not found at operation were presumably either normal or atrophic histologically, or were not present. This assumption is supported by our data, which show that the staining property of the parathyroid gland is directly related to its size and that the histologically adenomatous or hyperplastic gland stains more readily than the normal gland. This could be due to increased avidity of metabolically hyperactive, parathyroid cells for the dye. Conversely, glandular staining may simply be a function of increased cellular concentration in adenomatous or hyperplastic glands that lack the fat content of normal or atrophic glands. However, the glandular size and histology may vary independently in relation to tissue staining. Dudley (1971) noted intense staining of parathyroid adenomas, while normal glands were a dusky slate blue. While we can confirm these observations, we chose to classify as unstained any parathyroid glands in which a definite colour change was not obvious. We considered that such minimal staining of glands was not adequate for localization at operation.

Thiazide dyes (methylene blue, toluidine blue, thionine, Azur A) are taken up preferentially in certain tissues of the body (Dudley, 1971; Normann and Normann, 1972). The tissue distribution of toluidine blue has been studied most extensively. This dye localizes in parathyroid, heart, pancreas and thyroid tissue, although there appear to be differences between species (DiGiulio and Morales, 1969; Archer et al., 1972). Differing rates of tissue clearance are a useful characteristic of the dye (DiGuilio and Morales, 1969; Mortenson and McRae, 1970; Archer et al., 1972). This permits prolonged searching for stained parathyroid glands, while the colour of the thyroid has already returned to normal (Hurvitz et al., 1968; (Tardy and Tenta, 1971). However, premature infusion of toluidine blue may result in loss of parathyroid staining by the time the preliminary dissection of the neck is completed. Indeed, in an unpublished study we have found that 45–60-minute infusions of toluidine blue, terminated 15 minutes before parathyroid visualization, resulted in more frequent parathyroid staining than similar dye infusions concluded 2–4 hours prior to visualization. We used this experience when methylene was substituted for toluidine blue, because of the reported cardiotoxicity of the latter dye (Pridgin et al., 1969; Yeager and Krementz, 1969; Singleton and Allums, 1970). Methylene blue was found to be approximately equally effective in parathyroid localization during operation for primary hyperparathyroidism. Other similarities of these dyes are characteristically transient staining of muscle and thyroid tissue, as well as their ability to stain pancreatic tissue. Indeed, methylene blue has been reported to stain deeply a tumour of the pancreas secreting an insulin-like substance (Gordon et al., 1974).

Methylene blue infusion decreased the time needed for identification of the parathyroid glands. Staining of non-parathyroid tissue was limited to lymph nodes showing reactive hyperplasia and to abnormal thyroid tissue. This presented no problem, merely resulting in an occasional additional biopsy taken for frozen section. No complications attributable to methylene blue infusion were experienced. Therefore, we conclude that methylene blue administered by intravenous infusion is a safe effective method of localizing abnormal parathyroid tissue although it may occasionally also stain normal or atrophic glands significantly.

References

ARCHER E. G., POTCHEN E. J., STRUDER R. and SIEGEL B. (1972) Tissue distribution of ^{125}Iodine-toluidine blue in the rat. *J. Nucl. Med.* **13**, 85–91.

AURBACH G. D., MALLETTE L. E., PATTERN B. M., et al. (1973) Primary hyperparathyroidism. Recent studies. *Ann. Intern. Med.* **79**, 566–581.

BLACK W. C. and HAFF R. C. (1970) The surgical pathology of parathyroid chief cell hyperplasia. *Am. J. Clin. Pathol.* **53**, 565–579.

CASTLEMAN B. (1952) Tumors of the parathyroid glands. In: *Atlas of Tumor Pathology*, Fascicle 15. Washington DC, Armed Forces Institute of Pathology, p. 7.

DIGIULIO W. and LINDENAUER S. M. (1970) Use of tolonium chloride in localization of parathyroid tissue. *JAMA* **214**, 2302–2306.

DIGIULIO W. and MORALES J. O. (1969) The value of the selenomethionine Se 75 scan in preoperative localization of parathyroid adenomas. *JAMA* **209**, 1873–1880.

DOPPMAN J. L., HAMMOND W. G., MELSON G. L., EVANS R. G. and KETCHAM A. S. (1969) Staining of parathyroid adenomas by selective arteriography. *Radiology* **92**, 527–530.

DUDLEY N. E. (1971) Methylene blue for rapid identification of the parathyroids. *Br. Med. J.* **2**, 680–681.

EGDAHL R. H. (1970) Surgery of the parathyroid glands. *Surg. Gynecol. Obstet.* **130**, 901–909.

GORDON D. L., AIRAN M. C., SCHWARTZ M. A. and MARTINEZ C. J. (1972) The significance of a change in serum calcium following parathyroidectomy. *Chicago Med. Sch. Q.* **31**, 23–25.

GORDON D. L., AIRAN M. C. and SUVANICH S. (1974) Visualization of an insulinoma using methylene blue. *Br. J. Surg.* **61**, 363–364.

HAFF R. C., BLACK W. C. and BALLINGER W. F. (1970) Primary hyperparathyroidism: changing clinical surgical and pathological aspects. *Ann. Surg.* **171**, 85–92,

HURVITZ R. J., HURVITZ J. S. and MORGENSTERN L. (1967) *In vivo* staining of the parathyroid glands and pancreas. *Arch. Surg.* **95**, 274–277.

HURVITZ R. J., PERZIK S. L. and MORGENSTERN L. (1968) *In vivo* staining of the parathyroid glands. *Arch. Surg.* **97**, 722–726.

KLOPPER P. J. and MOE R. E. (1966) Demonstration of the parathyroids during surgery in dogs, with preliminary report of results in some clinical cases. *Surgery* **59**, 1101–1107.

MORTENSON R. A. and MCRAE J. (1970) Toluidine blue-O and its analogs as parathyroid and pancreatic scanning agents. *Arch. Surg.* **100**, 710–713.

NORMANN E. and NORMANN T. (1972) Uptake of ^{3}H-labelled commercial toluidine blue and subfractions (thionine, toluidine blue, and azar A) in the parathyroids of rabbits. *Scand. J. Clin. Lab. Invest.* **29**, 403–406.

PRIDGIN W., RICHARDSON R., CHAPPELL F., and PRIDGEN S. A. (1969) Primary hyperparathyroidism: diagnosis and surgical management. *South. Med. J.* **62**, 503–506.

RIENHOFF W. F., RIENHOFF W. F., BRAWLEY R. K. and SHELLEY W. M. (1968) The surgical treatment of parahyperthyroidism. *Ann. Surg.* **168**, 1061–1074.

SHIMKIN P. M. and POWELL D. (1973) Parathyroid hormone levels in thyroid-vein blood of patients without abnormalities of calcium metabolism. *Ann. Intern. Med.* **78**, 714–716.

SINGLETON A. O. and ALLUMS J. (1970) Identification of parathyroid glands by toluidine blue staining. *Arch. Surg.* **100**, 372–375.

STRAUS F. H. and PALOYAN E. (1969) The pathology of hyperparathyroidism. *Surg. Clin. North Am.* **49**, 27–42.

TARDY M. E. and TENTA L. T. (1971) Parathyroid identification with toluidine blue. *Laryngoscope* **81**, 1455–1461.

YEAGER R. M. and KREMENTZ E. T. (1969) Toluidine blue in identification of parathyroid glands at operation. *Ann. Surg.* **169**, 829–838.

Br. J. Surg. Vol. 62 (1975) 750–752

Selective surgery for abdominal stab wounds

A. THAVENDRAN, A. VIJAYARAGAVAN AND RUDRA RASARETNAM*

SUMMARY

The value of selective surgery for abdominal stab wounds was assessed in a prospective study of 226 patients admitted over an 18-month period. Two died soon after admission and before operation, the indications for which were signs of peritoneal irritation or haemorrhage, evisceration of bowel and omental protrusion. Of the 226 patients, 113 were selected for immediate surgery, which was carried out within 3 hours of admission. There were 12 deaths (10·6 per cent). Of the 111 patients initially selected for observation, 47 (42·3 per cent) underwent delayed operation with 4 deaths (8·5 per cent), but in only 1 (2·1 per cent) of these patients could the delay have influenced the adverse result. There were no deaths in the 64 patients treated conservatively. The overall mortality rate for patients who were initially selected for observation was 3·9 per cent.

One hundred and fifty patients underwent laparotomy, positive findings justifying operation being present in 134 (89 per cent). Six patients required thoracotomy for concomitant thoracic injuries, including 2 patients who required cardiorraphy. Four other patients required combined thoracic and abdominal exploration. The selection of patients for either conservative or operative management was based entirely on clinical criteria; abdominal X-rays were not helpful in the early diagnosis of visceral lesions. The indications for operation were evident within 12 hours of admission in 156 of the 160 patients who were treated surgically.

A substantial reduction in the incidence of 'negative laparotomy' can be made by this process of selection, and without an associated increase in the morbidity and mortality rates.

UNTIL recently laparotomy has been advocated for all stab wounds of the abdomen where peritoneal penetration is present, or suspected of being present, for fear that without exploration, visceral injury requiring repair might be overlooked. In view of the large number of negative explorations that were carried out, Shafton (1960) advocated a policy of selective conservative management, a view that has slowly gained acceptance in some centres, since with careful clinical evaluation many unnecessary operations are avoided and without an associated increase in the morbidity and mortality rates (Rothschild and Treiman, 1966; Ryzoff et al., 1966; Friedman, 1968; Richter and Zaki, 1970). Controversy, however, still exists, with many surgeons favouring routine laparotomy in all abdominal stab wounds in view of the difficulties of early diagnosis of visceral lesions (Goldman et al., 1962; Maynard and Oropeza, 1968).

This paper is based on a prospective study of patients admitted to the Accident Service of Colombo General Hospital during the 18-month period commencing in May 1972. A policy of selective surgery for abdominal stab wounds was practised, the criteria for which are described below.

Patients and methods

Two hundred and twenty-six consecutive patients with abdominal stab wounds were admitted during the period of the trial; 72 also had thoracic injuries. There were 213 men and 13 women, with ages ranging from 9 to 73 years, the maximum incidence being in the third and fourth decades. Multiple stab wounds were not unusual and were associated with a rising mortality rate, particularly when distributed over the whole of the trunk. In the critically ill patient with multiple stab wounds who required immediate exploration to arrest haemorrhage there was a danger that a second significant wound might be overlooked, as happened in 1 patient who underwent immediate cardiorraphy for cardiac arrest due to tamponade, only to succumb 3 hours later from an unrecognized injury to the right kidney.

In abdominal injuries no one sign could be said to be diagnostic, with the possible exception of hypotension, in the early phase after injury, but a reasonable assessment could be made on the whole clinical picture. Abdominal guarding was frequently present, particularly around the external wound, but in the absence of visceral injury it tended to be localized and to regress with time. Rigidity and abdominal distension were usually late in onset and indicated peritonitis. Bowel sounds were almost invariably present soon after injury even in the presence of visceral perforation. On the other hand, they were absent in only 11 patients, 10 of whom had visceral injuries, while the eleventh was transferred to this hospital 51 hours after being stabbed, and had ileus due to a retroperitoneal haematoma. Stab wounds of the lower chest, particularly on the left, were often associated with upper abdominal tenderness and guarding, and were the most difficult diagnostic problems. Taking into account the interval since injury, repeated clinical examination, preferably by the same individual, was the best aid for accurate diagnosis. Abdominal X-rays were useless, as in no case with positive radiological features was the diagnosis or the necessity for exploration not already obvious on clinical grounds.

The indications for laparotomy were signs of peritoneal irritation or haemorrhage, a systolic blood pressure of 80 mm Hg or less and evisceration of

---

* Colombo General Hospital, Sri Lanka.
Present address of A. Thavendran: General Hospital, Chilaw, Sri Lanka.
Present address of A. Vijayaragavan: General Hospital, Ratnapura, Sri Lanka.

bowel and omental protrusion. There was some doubt early in the trial as to whether omental protrusion alone should be a definite indication for laparotomy, but analysis of the results shows that these patients have the same incidence of visceral injury as the rest of the patients who underwent laparotomy (*Table I*). The presence of any of these criteria was an indication for immediate exploration, the remainder being kept under observation for the possible later development of such criteria.

Resuscitation was carried out in all patients before operation, with the exception that when significant haemorrhage was suspected, exploration and resuscitation were carried out simultaneously. A systolic blood pressure of 80 mm Hg or less in patients with abdominal trauma who were seen within an hour of injury was considered indicative of a vascular lesion, requiring immediate exploration.

Seventy-two patients had thoraco-abdominal injuries, 37 having separate external wounds in the chest and abdomen, the remaining 35 having diaphragmatic penetration, but only one of the latter presented with a hernia. All but one of the patients with diaphragmatic penetration had external chest wounds, and although this occurred more frequently with lower thoracic stab wounds, it was also present in 8 patients with wounds in the upper thorax.

Results

Two patients admitted in a critical state died before operation; one was admitted with absent vital signs due to perforating injuries of the heart, diaphragm, liver, stomach and pancreas, and the other patient was in severe shock due to an aortic injury.

One hundred and sixty of the 226 patients underwent surgery: 150 laparotomies, 6 thoracotomies and 4 thoracolaparotomies (*Table II*). Laparotomy was associated with a 7·3 per cent mortality rate, while combined thoracic and abdominal exploration carried a prohibitive mortality of 75 per cent. One hundred and thirteen of the patients had criteria justifying immediate exploration which was carried out within 3 hours of admission. There were 12 deaths in this group, a mortality of 10·5 per cent, but this figure also includes the patients who required thoracotomy. The remaining 111 patients were initially selected for conservative treatment, but 47 of them subsequently required abdominal exploration, which was carried out between 3 and 22 hours after admission (*Table III*). There were 4 deaths in the patients who underwent delayed operation (8·5 per cent), the operations in these 4 being carried out between 6 and 10 hours after admission. These patients form the crucial group in the evaluation of selective surgery for abdominal stab wounds. In only one of them could the delay have affected the result—a patient with a stab wound in the third right intercostal space in the axillary line who had no evidence of an abdominal lesion at admission but 7 hours later required exploration for a penetrating liver injury. When the clot overlying the hepatic wound was dislodged brisk haemorrhage recommenced and was controlled by suture. He died 3 days later because of lack of blood for transfusion, and the result may well have been different had it been available. The delay of up to 10 hours before surgery had no bearing on the other 3 deaths. One patient with multiple stab wounds was transferred to this hospital 51 hours after being attacked; he presented with abdominal distension, ileus and incipient uraemia due to a retroperitoneal haematoma, and he had a cardiac arrest on the operating table. Another patient died 14 days postoperatively of septicaemia due to infection in a retroperitoneal haematoma. The final patient, who had a lower thoracic stab wound, was found at laparotomy to have an anterior gastric wound which had not penetrated the lesser sac. He bled to death from an unrecognized mucosal tear on the posterior gastric wall and must be considered a technical error.

Table I. SIGNIFICANCE OF EVISCERATION OF BOWEL AND OMENTAL PROTRUSION

	Omental protrusion	Evisceration of bowel
No. of patients	48	10
No. died	1	0
Operation	47	10
Operative deaths	0	0
Negative laparotomy	5	2

Table II: MANAGEMENT

	All abdominal injuries			Thoraco-abdominal injuries		
	No.	Died	%	No.	Died	%
Total	226	18	7·9	72	10	13·8
No operation	66	2	3·0	17	2	11·7
Laparotomy	150	11	7·3	45	3	6·6
Thoracotomy	6	2	33·3	6	2	33·3
Thoracolaparotomy	4	3	75·0	4	3	75·0
Negative laparotomy	16	0	—	4	0	—

The figures for thoraco-abdominal injuries are also included in those for all abdominal stab injuries.

Table III: MORTALITY IN RELATION TO THE TIME INTERVALS BETWEEN INJURY AND ADMISSION AND OPERATION

	Injury to admission		Admission to operation		
Time	No.	Died	No.	Died	Negative laparotomy
0–30 min	65	6	7	4	1
31–60 min	49	3	26	4	2
1 h 1 min–3 h	43	1	80	4	6
3 h 1 min–6 h	46	5	29	0	4
6 h 1 min–12 h	15	1	14	4	2
12 h 1 min–36 h	2	0	4	0	1
Over 36 h	2	1	0	0	0
Not known	4	1	0	0	0

Negative laparotomy

A retrospective analysis was made of all the patients undergoing exploration in an effort to determine whether operation had been necessary. Laparotomy was classed as necessary if a visceral lesion requiring repair was present, if haemostasis had to be effected or if the peritoneal cavity contained more than 250 ml of blood irrespective of whether the source of bleeding was identified or even if active bleeding had ceased. An operation was considered to be a 'negative laparotomy' when no visceral lesion required repair, as in superficial liver injuries that had ceased bleeding, or if the peritoneal cavity contained less than 250 ml of blood without evidence of continuing haemorrhage. Peritoneal penetration alone was considered to be a negative laparotomy, as was a retroperitoneal haematoma not requiring haemostasis. Sixteen of the 150 laparotomies (10·6 per cent) were judged by these criteria to be negative, and it is interesting that they were evenly spaced out throughout the whole 22-hour period after admission during which the operations were performed (*Table III*).

Length of hospital stay

The average duration of hospital stay for patients treated conservatively and by operation was 5 and 12 days respectively. The morbidity in the conservative group was negligible.

Discussion

Mandatory laparotomy has been accepted practice for penetrating abdominal wounds for many years. In a retrospective analysis Shafton (1960) found that in the absence of definite clinical criteria there was a high incidence of negative explorations in abdominal stab wounds. The policy of selective surgery can be justified only if there is no mortality and reduced morbidity in patients treated conservatively, and also that any delay in operation inherent in this policy of 'wait and see' does not adversely affect the result. Subsequent reports have confirmed that these objectives may be achieved by careful clinical evaluation (Ryzoff et al., 1966; Cameron, 1970; Richter and Zaki, 1970). In the present series of 226 patients clinical evidence to warrant surgery was present at the time of admission in 113 (50 per cent), and in 43 of the 47 patients who underwent delayed surgery it was present before 12 hours had elapsed. In only 4 patients were the signs so inconclusive that operation had to be delayed up to 22 hours. Delay could be incriminated in the result in only 1 case who might have recovered if blood had been available at some time during the 3-day postoperative period. Sixty-four patients (28·2 per cent) were treated conservatively without any fatality and with reduced morbidity and period of hospital stay.

The selection of patients for either conservative or operative treatment is the most difficult aspect of management. Goldman et al. (1962) and Maynard and Oropeza (1968), who advocated mandatory laparotomy, found that 57 and 42 patients in their respective series who had negative physical signs had visceral injuries at operation, and consequently doubted the value of clinical assessment. The injection of radio-opaque solutions into the wound (Smithwick et al., 1968; Haddad et al., 1970) and exploration of the wound under local or general anaesthesia (Goldman et al., 1962; Roberts and Lavelle, 1966; Roy, 1974) have been used in an effort to delineate peritoneal penetration, and thereby reduce the incidence of negative laparotomy, but there is no convincing evidence that it will make a substantial reduction as the more important reasons for operation are not assessed. Negative laparotomy is inevitable in penetrating abdominal trauma, even with selective surgery, but its incidence can be reduced with such evaluation. Attempts to reach statistical perfection must be forsaken, and a negative exploration rate of 10 per cent seems reasonable. The argument against mandatory laparotomy would be less impressive were it not for the complications associated with it. Emergency surgery in an unprepared patient carries a slight morbidity and mortality, and a rate as high as 6·3 per cent for the latter has been reported (Maynard and Oropeza, 1968).

Acknowledgements

We have pleasure in thanking the resident surgeons of the Accident Service, Colombo General Hospital, for allowing us to include patients treated by them; Mr Y. R. Karunaratne for help with the analysis of data; and Miss Nafeeza Mousajee and Miss B. Ranatunga for secretarial help.

This work was partly supported by a grant from the National Science Council of Sri Lanka.

References

CAMERON C. T. M. (1970) Stab wounds of the abdomen. *J. R. Coll. Surg. Edinb.* **15**, 330–336.

FRIEDMANN P. (1968) Selective management of stab wounds of the abdomen. *Arch. Surg.* **96**, 292–295.

GOLDMAN L. I., DE LAURENTIS D. A. and ROSEMOND G. P. (1962) Penetrating abdominal wounds in a civilian population. *Am. J. Surg.* **104**, 46–51.

HADDAD G. H., PIZZI W. F., FLEISHMANN E. P. and MOYNAHAN J. M. (1970) Abdominal signs and sinograms as dependable criteria for selective management of stab wounds of the abdomen. *Ann. Surg.* **172**, 61–67.

MAYNARD A. DE L. and OROPEZA G. (1968) Mandatory operation for penetrating wounds of the abdomen. *Am. J. Surg.* **115**, 307–312.

RICHTER R. M. and ZAKI M. H. (1970) Selective conservative management of penetrating abdominal injuries. *Surg. Gynecol. Obstet.* **130**, 677–681.

ROBERTS G. and LAVELLE E. (1966) The management of stab wounds of the abdomen and thorax. *Br. J. Surg.* **53**, 88–93.

ROTHSCHILD P. D. and TREIMAN R. L. (1966) Selective management of abdominal stab wounds. *Am. J. Surg.* **111**, 382–387.

ROY A. D. (1974) Abdominal injuries. *Br. Med. J.* **4**, 335–336.

RYZOFF R. I., SHAFTON G. W. and HERBSMAN H. (1966) Selective conservatism in penetrating abdominal trauma. *Surgery* **59**, 650–653.

SHAFTON G. W. (1960) Indications for operation in abdominal trauma. *Am. J. Surg.* **99**, 657–664.

SMITHWICK W. III, GERTNER H. R. and ZUIDEMA G. D. (1968) Injection of Hypaque (sodium diatrizoate) in the management of abdominal stab wounds. *Surg. Gynecol. Obstet.* **127**, 1215–1224.

Br. J. Surg. Vol. 62 (1975) 753–756

Reviews and notices of books

Handbook of Obstetrics and Gynaecology

Ralph C. Benson, Portland, Oregon. Fifth edition. 178 × 105 mm. Pp. 770+ix. Illustrated. 1974. Los Altos, California: Lange Medical Publications. $8.

This is a well-produced, convenient, pocket-sized book with clear print and numerous illustrations which covers the whole field of obstetrics and gynaecology in just under 800 pages. It provides a great deal of information about many topics in a rather superficial fashion yet gives no references to the literature or suggestions for further reading.

As the Preface points out, it is meant to supplement rather than substitute for more complete textbooks on the subject, but at the same time it is not written as a critical digest. Almost everything gets a mention, but sometimes little more than that. Methods of diagnosis or treatment are sometimes listed rather uncritically so that although an uninformed reader might know what was available he would not know what was appropriate.

Perhaps these comments are hypercritical, for the book certainly provides much information about obstetrics and gynaecology and does refer to many recent advances. Some parts are particularly good, including chapters on the emotional aspects of pregnancy and psychosomatic problems in gynaecology. The concise and up-to-date section on contraception is also first rate. However, nowadays, when obstetricians try to avoid performing difficult vaginal delivery, it is surprising that the sections on the management of abnormal labour should pay so much attention to describing many different types of obstetric forceps, as well as various obstetric manipulations now rarely used. The author's statement that classic Caesarean section will often be performed for placenta praevia or in obstetric emergencies such as abruptio placentae or prolapsed cord is at variance with the views of most obstetricians in this country, as would be his recommendation that routine appendicectomy should be performed at Caesarean section.

Some of the gynaecological approaches recommended in the book also appear to differ from current British practice. For example, in the investigation of the patency and function of the Fallopian tubes in infertile women, pride of place is given to insufflation, while hysterosalpingography is only mentioned very briefly, and laparoscopy not at all in this section.

The value of this book is that it allows the reader to skim through a wide-ranging but superficial account of obstetrics and gynaecology in a relatively short time. Practising physicians might benefit from considering the approaches mentioned in it, but medical students in this country could find it difficult to absorb and not always in line with their clinical teaching.

A. C. TURNBULL

Fibre-optic Endoscopy

P. R. Salmon, Bristol. 215 × 155 mm. Pp. 237+xiii. Illustrated. 1974. Tunbridge Wells: Pitman Medical. £4·50.

This is an essential manual for all those starting out in endoscopy and of great practical help to those already established in the practice. It will be invaluable not only to clinicians but also to nurses and ancillary staff. Radiologists and pathologists will find it of interest as well. It is full of all the useful advice so often missing from books of this kind. Dr Salmon deals with all the important details in the setting up of an organization of an endoscopy service, and the care and maintenance of the expensive equipment. He also deals effectively with handling of tissues obtained during endoscopy, and there are helpful chapters on photography and the role of radiology in fibre-optic endoscopy. This is an excellent book that can be thoroughly recommended.

IAN MCCOLL

1974 Year Book of Surgery

Edited Seymour I. Schwartz, Rochester, et al. 235 × 155 mm. Pp. 525, with 172 illustrations. 1974. London: Lloyd-Luke. £9·60.

For those not familiar with the format of this series, this book is a potpourri of several hundred well-written abstracts of selected original papers of surgical interest. Each abstract is accompanied by a short avuncular comment on the merit and significance of the work. There is also a 20-page 'annual overview' which summarizes very briefly the developments thought to be most important by the six American professors of surgery who form the editorial team.

The amount of work needed to complete this volume must have been enormous. Was it worth it? Since much of the whole spectrum of surgery is covered, no single subject can be dealt with in sufficient depth to be of interest to the specialist in that subject. However, the book will be useful to the man who is keen to keep abreast of subjects other than his own or who wants to fill in those embarrassing gaps in knowledge which we all suffer when we miss an important article in one of the common journals which everyone else seems to have read.

One or two criticisms have to be made. First, there are some surprising omissions, e.g. the virtual absence of reports on gastric cancer. Next, it appears that only the English literature was considered and it is difficult to believe that no surgical advances were described in other languages. Finally, the title of the book is a trifle misleading since the literature up to February 1974 only is reviewed. Nevertheless, it provides a relatively painless way of keeping up-to-date. Prospective purchasers should note that subjects such as urology, neurosurgery and orthopaedics are dealt with in other 'Year Books'.

ALAN G. COX

The Faber Medical Dictionary

Edited Sir Cecil Wakeley, now revised by J. G. Bate, London. Second edition. 245 × 190 mm. Pp. 483. 1975. London: Faber and Faber. £6·95.

English being the accepted international language of science and medicine, a reliable and up-to-date reference work will always be needed by authors, secretaries and editors to maintain accuracy in what they write. Most of the existing medical dictionaries are American. This means that the special needs of British users are sometimes incompletely met. The new Faber now comes to their aid with a good clear explanation of nearly all essentials, especially the more recent arrivals in the medical vocabulary, such as antilymphocytic globulin, FDP's, Kveim's test, lincomycin and technetium. For those of more classical inclinations, there is the extensive etymological material that clearly explains for the interest and instruction of the red brick medical reader also the derivation of that large and still growing majority of medical terms for which the Greeks and Romans left us a concise and descriptive word basis. There is still much historical material, some of which borders on the archaic and even the mythological. Burn's blindness from sexual overactivity and Richardson's sign of persisting life in a supposed corpse both may have a kind of whimsical usefulness. Hairy tongue we mostly remember but never see, yet hairy-celled leukaemia has not been included. Chemoreceptor tissue is ably defined, but not chemodectoma. Perhaps it belongs in the fossa cároticum, mentioned in Malgaigne, but not located. Even with faults like these, which may worry overseas readers more than us at home, it is a fine effort, well produced, full of interest for browsing in, as well as for pouncing on when we need. It is good value at the price.

H. H. G. EASTCOTT

Reviews and notices of books

Surgical Forum—The Liver

Edited Rodney Smith, London. 215 × 135 mm. Pp. 163+x. 1975. London: The Butterworth Group. £2·80.

THIS volume brings together an international group of surgeons with an interest in different aspects of hepatic surgery. The book aims to capture the atmosphere of a surgical forum and each author presents a chapter after which the others are asked to comment.

In general the Editor, Sir Rodney Smith, has succeeded in his aim in that the book allows the reader a review of the approach of experts to the four subjects covered, namely cirrhosis of the liver and acute hepatic failure, liver transplantation, hepatic trauma and tumours of the liver. The book should be of value not only to the general surgeon but to specialists with an interest in liver surgery.

The chapter by Alexander Walt on hepatic trauma reflects the immense experience of the Detroit group and gives a balanced view of the subject. Professor Walt makes a strong case for the avoidance of routine T tube drainage for hepatic injury, but the evidence for the avoidance of T tube drainage in the major blunt injury requiring resection is not clear. The use of antibiotics in patients requiring resection is also somewhat scantily dealt with, but these are minor criticisms of an otherwise excellent contribution.

The chapter by Professor R. Y. Calne puts the case for liver transplantation and carries an authority which few people have the experience to question. Perhaps the case against auxiliary liver transplantation is too strongly made. The controversy relating to the wasting of the transplanted auxiliary liver has not been resolved and there is as yet no firm evidence that specific hepatotrophic factors exist. One may be a little concerned about the use of transplantation for various forms of liver cancer, but the chapter by John Dawson makes it clear that the current therapeutic approach to malignancy within the liver leaves much to be desired. Mr Dawson makes a balanced contribution but perhaps underemphasizes the possible value of chemotherapeutic agents used early after diagnosis in the asymptomatic patient.

The remaining chapter on cirrhosis of the liver and acute hepatic failure is from Professor Terblanche's group at Cape Town and outlines the approach of this experienced team, particularly in dealing with the problem of bleeding varices as a result of portal hypertension. The chapter is perhaps less valuable to the specialist in that the approach to problem areas is somewhat superficial. For example, it is a little disappointing to see the hepatorenal syndrome referred to as a complication of operation on cirrhotic patients without further clarification.

Perhaps the most enjoyable feature of this book is the comments at the end of each chapter. In particular, Professor Walt's criticisms carry the stamp of authority and wide experience. This is a book of value to generalists and specialists alike and succeeds in its aims of bringing the atmosphere of the forum to the reader.

L. H. BLUMGART

Prostheses and Rehabilitation after Arm Amputation

L. F. Bender, Michigan. 228 × 150 mm. Pp. 179+xv, with 76 illustrations. 1974. Springfield, Ill.: Charles C. Thomas. $12.50.

THIS little book deals with some of the problems resulting from either upper limb amputation or congenital arm deficiency, as seen in the United States. The causative factors and incidence are similar to those in the United Kingdom, viz. a high proportion being due to trauma (mostly industrial) and about 20 per cent congenital in origin, compared with 30 per cent in Britain.

It is surprising to note that out of 400 upper limb amputations seen by the author, only 9 were performed for lesions of the brachial plexus. He rightly advocates arthrodesis of the shoulder and above-elbow amputation for the complete lesion. The reviewer, however, does not agree with the recommended level of bone section given as 2½ inches above the end of the humerus. It should be at least 4½ inches otherwise the automatic elbow mechanism, used on British prostheses, cannot be incorporated.

Although there is a chapter on 'Levels of Amputation', it gives negligible guidance to surgeons concerning optimum levels. The disadvantages of long above-elbow and below-elbow stumps and of an elbow disarticulation are not stressed. The problems of fitting a wrist disarticulation are mentioned although these have been overcome in the United Kingdom.

Immediate postsurgical fitting is discussed together with the difficulties experienced. These are due mainly to the fact that the majority of the amputations are traumatic and the various receiving hospitals are not conversant with all the techniques involved. Nevertheless, when such fittings have been performed they have been quite successful. It is universally agreed that the sooner a prosthesis can be fitted the greater the chances of an amputee becoming two-handed again. Consequently, the author very rightly stresses the need for early fitting for bilateral amputees.

There is an excellent chapter on postoperative therapy and methods of performing numerous daily tasks one-handed.

The author has nothing new to offer for the relief of phantom pain although he states 'acupuncture warrants investigation'. More than two-thirds of the book are devoted to prosthetic fabrication, fitting and harnessing. Although the basic principles are similar there are major variations between the American and British techniques.

Mention is made of a variety of hands and other terminal devices including the widely accepted 'split-hook'. Credit for the myoelectric hand goes to the USSR, while the pioneer work in this field started in Britain is overlooked! There is, however, no indication of the acceptance rate among American amputees.

IAN FLETCHER

Ferguson's Surgery of the Ambulatory Patient

Edited Mark W. Wolcott, Salt Lake City, Utah. Fifth edition. 250 × 180 mm. Pp. 554+xv. Illustrated. 1974. Oxford: Blackwell Scientific Publications. £13·50.

DURING the past decade there has been a growing interest in 'day case' surgery in this country. The surgery of the ambulatory patient has advanced further in the United States than here not only because of the mutual problem of pressure on hospital beds, but because, as the Editor states in the introductory chapter, the growing cost to the individual patient in the United States 'has nearly priced the average citizen out of the health care market'.

Our ability to carry out an increasing range of surgical procedures without admitting the patient to hospital is largely due to the considerable advances in modern anaesthesia, which is discussed in the extremely informative chapter by Dr Edwin L. Rushia.

The selection of material for such a book must be extremely difficult and, by and large, the Editor is to be congratulated on the range of topics he has chosen. Not only are the usual procedures for 'minor surgery' described in detail, but there is important information dealing with the relatively minor surgical procedures which are often required for the satisfactory care of patients discharged from hospital following major surgery.

In a book with such wide coverage it is inevitable that a number of oddities will appear. To find axillary boils ('hidradenitis suppurative of axilla'!) in the same chapter separated by only a few pages from fractures of the scapula, including its rarer forms, is perhaps somewhat surprising. Although it is doubtful whether British surgeons would find it acceptable to treat in an outpatients' department malignant disease of the oral cavity, the chapter on cryosurgery by Dr Andrew Gage does open up important new vistas. The chapter on the breast has a number of surprises: can intraductal papillomas be dealt with satisfactorily in an outpatients' department, and is this the right book in which to describe in detail the technique of an operation for gynaecomastia?

In spite of these occasional excesses, the book contains a vast amount of serious practical information. The illustrations are simple and clear. A young house surgeon, casualty officer or general practitioner wishing to continue the active personal care of his patients following major surgery would do well to peruse this book and keep it on his shelf.

L. KESSEL

Reactions to Injury and Burns and Their Clinical Importance

S. Sevitt, Birmingham. 210 × 140 mm. Pp. 255 + vi. Illustrated. 1974. London: William Heinemann Medical Books. £4·25.

RECENT monographs concerning the response to injury have tended to deal with the more general metabolic features which follow injury, perhaps because this is the important feature of clinical management which has been most topical. There has therefore been a need for an approach to the subject which has taken a broader view of the systematic and general reaction of the body to injury. This is the purpose of this monograph by Dr S. Sevitt.

The first part deals with the statistics of accidental injury, the factors related to death from injury and the normal homeostatic responses, and this provides the base for the subsequent sections on the effect of injury on tissues such as the lungs, liver, kidney and central nervous system. Much of the descriptive element and the discussion revolves around severe trauma associated with shock or hypoperfusion. The chapter on endocrine responses in particular is comprehensive and is a useful review of the many changes which are found in the injured patient.

The last section details changes in coagulation, fat embolism and immunity, cellular and humoral, in the traumatized or burned patient. This is an especially useful part of the book which deals unusually with aspects of trauma not normally discussed in relation to the metabolic changes, and this adds considerably to the breadth of the topic being covered. It was, however, tantalizing to find points raised which could not be followed up in the rather brief bibliography supplied, but one must accept this in a relatively concise work such as this. This book will be of use to any doctor concerned with the management of the injured or severely ill patient.

R. G. CLARK

Surgery Annual: 1974 Vol. VI

Series editor: Lloyd M. Nyhus, Chicago, Illinois. 236 × 165 mm. Pp. 489 + xii. Illustrated. 1975. Hemel Hempstead: Prentice-Hall International. £12·95.

THIS annual review of surgery is now well established in its sixth year. The Editor has selected 31 contributors, mostly from the United States, but has included several South Africans, a Finn and Professor David Johnston, now at Bristol. The 20 chapters are widely ranging indeed; the spectrum stretches from chapters on basic topics such as metabolic aspects of shock, techniques of blood flow measurements and sickle cell disorders, through the applications of computers to patient care, paediatric anaesthesia and gastric mucosal anomalies to general surgical topics which include the management of pancreatic cancers. Under orthopaedics there are chapters on hand injuries, the surgery of rheumatoid arthritis and total knee replacement arthroplasty. Highly specialized subjects such as carbon dioxide laser surgery in laryngeal disease and intracranial infections give a fascinating account of the advances in these fields. Of particular interest are the excellent contributions by Leslie Wise on controversies in the management of so-called 'early' breast cancer, and a discussion by John Madden on the controversial topic of electrocoagulation in the treatment of cancer of the rectum, which includes useful advice on the exact technique of this method and the indications for its use.

This volume, like its predecessors, is beautifully produced and illustrated with up-to-date and copious references. Being so widely based, it will be particularly attractive to general surgeons (who are always keen to keep abreast of current work in adjacent fields) and to candidates for higher surgical degrees, rather than to our somewhat less fortunate colleagues, the 'super-specialists'.

HAROLD ELLIS

Ventilatory and Phonatory Control Systems

Edited Barry Wyke, London. 230 × 155 mm. Pp. 531 + xviii. Illustrated. 1974. London: Oxford University Press. £6.

SMALL symposia, whether they be national or international, are usually of considerable value to the participants most of whom have been selected for their special interest in the subject under discussion. Whether a much wider audience exists justifying publication of the proceedings of such meetings is largely dependent on the importance of the topic and the speed with which the papers can be printed in an acceptable manner. Unhappily, 3 years after presentation is too long even for the most original and important contributions—and this meeting was held in January 1972! Since the editor personally thanks the participants for promptness in producing their papers the blame for delay must lie with the publishers. This is sad, for although the quality of reproduction of illustrations is poor this book represents exceedingly good value for money.

Twenty-five papers were given by contributors drawn from many countries and a wide variety of disciplines, ranging from respiratory physiology to phonetics. Their collective ambition was to evaluate the current position and possible lines of future research in the related fields of ventilatory and phonatory control. Despite the vastness of this undertaking they succeeded remarkably well, and the division of the various papers into four sections assists the reader in digesting the mass of facts and figures which appear to be an integral part of each paper.

An additional bonus is the inclusion of the free discussions which followed individual communications. All show evidence of meticulous editing, whilst the addition of appropriate references suggests that some of the delay in publication may be related to this section of the book.

All who are interested in the mechanisms which control breathing, speaking and singing will find this book a valuable source of information and ideas. Whether it will still stimulate new lines of research 3 years after its original conception is more doubtful, but in view of its modest price and original integration of multidisciplinary expertise it is certainly worth buying.

D. F. N. HARRISON

The Systematic Manifestations of Inflammatory Bowel Disease

Edited William M. Lukash and Raymond B. Johnson, Bethesda, Maryland. 228 × 152 mm. Pp. 356 + xii. Illustrated. 1974. Springfield, Ill.: Charles C. Thomas. $15.50.

THIS work will be of interest to the *cognoscente* because of the surprises it contains and the occasional lacunae; it would be unwise to recommend it to those without experience. The first surprise comes early: ulcerative proctitis, it is stated, is a relatively uncommon form of inflammatory bowel disease. This is hardly the experience here; perhaps populations differ, for the book is based on a symposium of United States Army doctors. Perhaps it reflects the physician orientation which obtrudes elsewhere, for proctitis may be seen more often in surgical clinics whence patients are referred as cases of 'bleeding piles'. This orientation is dominant in the attitude to therapy, an attitude hardly aggressive in character; of this the reader becomes particularly aware in the chapter on toxic megacolon, for its whole tenor is towards conservative treatment with little appreciation that the mortality of this condition can be contained only by recognition of bowel disintegration, with appropriate surgical action, before dilatation has developed (moreover none of the four contributors to this chapter is a surgeon). Elsewhere 'joint symptoms are seldom of sufficient severity to require surgery' must be the attitude of a softline therapist rather than the activist who knows from experience that joint trouble is usually an additional factor indicating that the time for surgery has arrived.

Some of the lacunae are minor, such as the omission of Crohn's stomatitis, and, in the chapter on cutaneous manifestations, those stigmata of prolonged severe disease, the striae 'non'-gravidarum seen in relation to the extensor surfaces of knees and elbows, and the skin attenuation on the digits of those with persistent hypoproteinaemia. Perhaps these conditions have not come the authors' way (the author of the chapter on differential diagnosis states that he has never seen tuberculosis of the bowel, or has failed to recognize it).

A comprehensive chapter on radiographic features provides useful 'visual' differential diagnoses; here numerous conditions including parasitic infestations are presented, some of which would hardly spring to mind for diagnostic exclusion, but lymphoma is omitted. More importantly, the simulation of diverticulitis by Crohn's disease of the sigmoid and that of terminal ileitis by chronic appendix abscess are conspicuous by their absence. A more considerable omission is the failure to appreciate that ischaemic colitis is bound to inflammatory bowel disease if only because it can masquerade as ulcerative or Crohn's colitis. Moreover, it is not confined to the elderly and retired, but must sometimes affect more active echelons, even generals less celebrated than Eisenhower, whose case history is fully exposed in the first chapter as an exemplar of Crohn's disease.

B. N. BROOKE

Atlas of Orthopaedic Surgery. Volumes 1 and 2

L. A. Goldstein and C. Dickerson, New York. 280×215 mm. Vol. 1: pp. 524+xiv; Vol. 2: pp. 592+xiv; 1674 illustrations. 1974. London: Henry Kimpton. £41·55.

THIS beautiful production is nearly a winner, but not quite. It falls between three stools. It is not a highly technical instruction book like the AO manual on fracture treatment, it is not a vade-mecum with a comprehensive commentary like Campbell and it is not a friendly but highly personal and subjective guidebook like Couzens. Yet in so many ways it is splendid. The layout is spacious, the type clear, the paper opulent and the binding sturdy. Most of the 1674 illustrations are enormously elegant, the references at the end of each section are catholic and helpful and the index of subjects and authors at the end is clear and comprehensive.

However, there are snags. In a book of this magnitude the most obvious is lack of diversity. Often only a single procedure is described for each disorder, and when the condition is as common and controversial as recurrent anterior dislocation of the shoulder this seems surprising. The somewhat meagre general discussion which opens each section might well have been expanded to include justification of the particular operation selected. The drawings delight the eye, but not all contain the detail which would make lengthy commentary superfluous—it is a pity that some of the acres of blank space have not been employed in providing more substantial verbal support. Consistency in illustrating always the right arm and right leg shows a perceptive awareness of the trainee's problems, so it is surprising that within the space of a few pages (759–65) the lower limb lies first from right to left, then vertical and finally from left to right.

Much of this criticism is mere carping. No work could maintain throughout the high standards of some sections, such as that on scoliosis, and no first edition of so ambitious a nature could be without blemish. These two volumes will be invaluable to residents, registrars and to many established surgeons. They represent immense effort and are an enormous achievement; they may be the prelude to a brilliant second edition.

A. GRAHAM APLEY

Symposium on Management of Cleft Lip and Palate and Associated Deformities. Volume 8

Edited Nicholas G. Georgiade, North Carolina. 280×220 mm. Pp. 324+xiii, with 685 illustrations. 1974. London: Henry Kimpton. £20·20.

THIS volume records the transactions of a symposium sponsored by the Educational Foundation of the American Society of Plastic and Reconstructive Surgeons. It contains 53 monographs written by the contributors, who include representatives of all the disciplines which share the responsibility of treatment of these complex deformities. The material includes anatomy, aetiology, general management, speech pathology, otology and orthodontics besides the surgery of primary repair and secondary correction, together with a good historical review of the development of this subspeciality of plastic surgery. All the disciplines concerned will find much of general interest and something of their own special contribution.

In the realm of surgical treatment the techniques advocated understandably bear the stamp of the preference of the individual contributors, and the inexperienced might find a choice difficult to make, but the trend of current thinking comes through, and those already experienced will find valuable the suggestions of the protagonists of alternatives. The editor has done well to produce a volume with an even high standard of presentation which is unavoidably a potential difficulty in a multi-author book. The illustrations are abundant and lucid, making for easy understanding of the intricacies of operative techniques. The production of the volume is of a very high quality; in some of the chapters the bibliography could have been extended with advantage.

DAVID MATTHEWS

Cardiac Arrest and Resuscitation

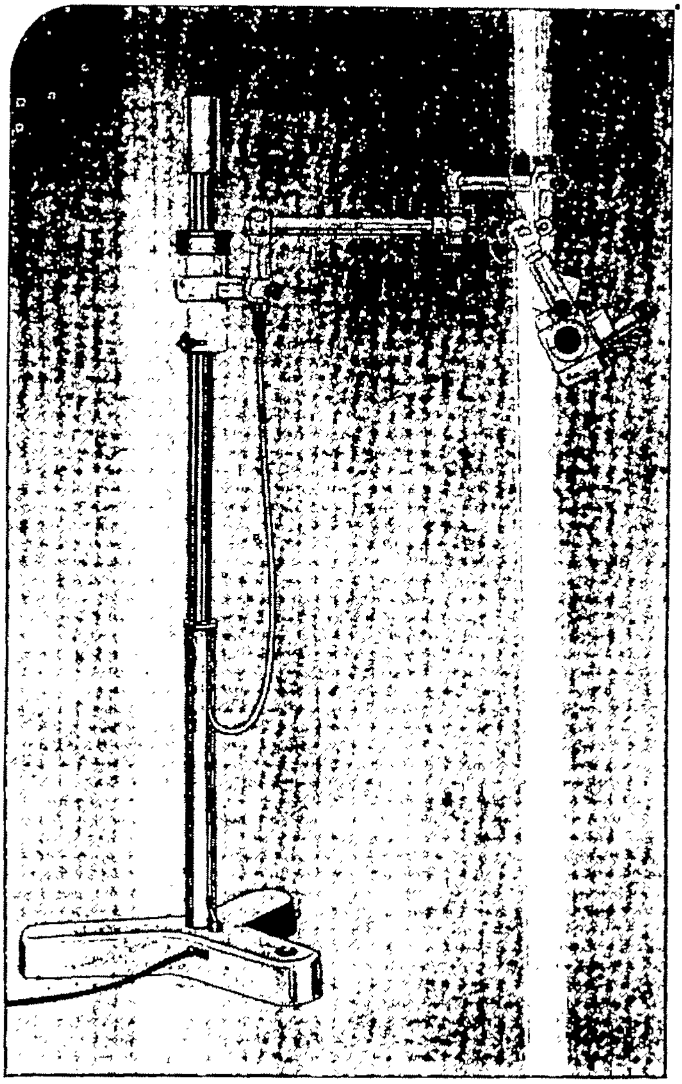
Hugh E. Stephenson, Columbia, Missouri, Fourth edition. 250×180 mm. Pp. 998+xviii, with 379 illustrations. 1974. London: Henry Kimpton. £22·55.

No improvement in life expectancy has been achieved in adult white males in the United States in this century despite medical advances. This lack of progress is to a considerable extent a consequence of the coronary epidemic which annually claims half a million lives in the United States and over 130 000 in England and Wales. Most of these deaths occur outside hospital. Drowning, electrocution, surgery, therapeutic agents, anaesthesia, etc., contribute to the total who die suddenly.

This admirable book provides a comprehensive current review of these topics, adding considerable new information since the last edition in 1969. A distinguished team of contributors from various disciplines assesses the detection and prevention of risk factors and the mechanism and pathophysiology of arrest. Resuscitation techniques are evaluated, including developments in pacing, circulatory assist by inter-aortic balloon pulsation and progress towards an effective artificial heart. Practical details are provided on equipping and training mobile resuscitation units and should encourage their hitherto sluggish development in the United Kingdom. The experience of stadium resuscitation units will interest sports medicine specialists and first aid personnel. The medicolegal aspects appertaining to the United States are dealt with in hair-raising detail and provide very sobering thoughts for a British reader.

The book provides a fine seam of reference sadly marred, however, by the frequent omission of dates in the text which renders mining the original more difficult; suggestions that the reader should refer to previous editions for references not included here are hardly likely to help those who have not managed to collect each edition. Inevitably a book by many contributors is patchy, chapters varying from excellence to a folksy anecdotal style. It is expensive (£22·55) and cumbersome. Nevertheless, it contains important material and should at least be dipped into by those likely to encounter cardiac arrest, namely all of us.

G. M. REES



SURGERY MICROSCOPE II

Another superb instrument from

CARL ZEISS JENA

This well established Surgery Microscope from VEB Carl Zeiss Jena has gained a well deserved reputation for it's reliability and all-round performance. It is extremely versatile, allowing complete freedom of movement. The working distance is 200-300 or 400mm. You'll be surprised at the competitive price of this popular microscope which incorporates optics of the highest quality. Remarkable value!

SPECIAL FEATURES INCLUDE:-

- ✻ Individually focussing eyepieces
- ✻ Rapid changing for two filters and five magnifications (5x, 8x, 12.5x, 20x, 32x)
- ✻ Observer eyepiece available
- ✻ Photographic attachments available.

Write or telephone for literature or demonstration on this instrument and others in the comprehensive VEB Carl Zeiss Jena Range.

CARL ZEISS JENA LTD., C.Z. Scientific Instruments Ltd.,
P.O. Box 43, 2 Elstree Way, Borehamwood, Herts WD6 1NH. *Tel: 01-953 1688.*
Manufactured by VEB Carl Zeiss Jena, Carl Zeiss Strasse 1, Jena, GDR.

INJURY

The British Journal of Accident Surgery

Editor, R. L. BATTEN, FRCS(Eng)

Injury provides a focal point of information for those engaged in the many fields of medicine which accident surgery involves. Contributions from all over the world provide well-organized and comprehensive coverage of every aspect of care of the injured. Original articles take up a large section of INJURY and, as accident surgery is so often concerned with the individual patient, reports of interesting and complex cases are included. To keep the reader informed of the latest progress, INJURY contains details of current research and of new drugs and medical instruments. Reviews of new books appear regularly and, of particular value in a field of medicine which often has a debt to other specializations, INJURY devotes some of its space to abstracts from a wide range of publications on related subjects.

Published Quarterly

Annual Subscription: £10·00 (post free)

Single Numbers: £3·00 (post free)

BURNS including Thermal Injury

The Journal of the International Society for Burn Injuries

Editor, J. E. LAING, FRCS

To counter the high mortality and morbidity caused by burn injuries needs the teamwork of a wide range of specialists: treatment of the patient can involve plastic, paediatric and orthopaedic surgeons, biologists, immunologists and bacteriologists, while the rehabilitation of the patient can need the efforts of occupational therapists, physiotherapists, psychiatrists and social workers. This new journal is published to foster the exchange of information amongst all those engaged in preventing and minimizing the effects of burn injuries. BURNS is sponsored by the International Society for Burn Injuries, whose aims are to transcend national boundaries in improving the prevention and care of burns by education, research, practical advice and assistance, and the encouragement of cooperation between all countries and all specialists.

Published Quarterly

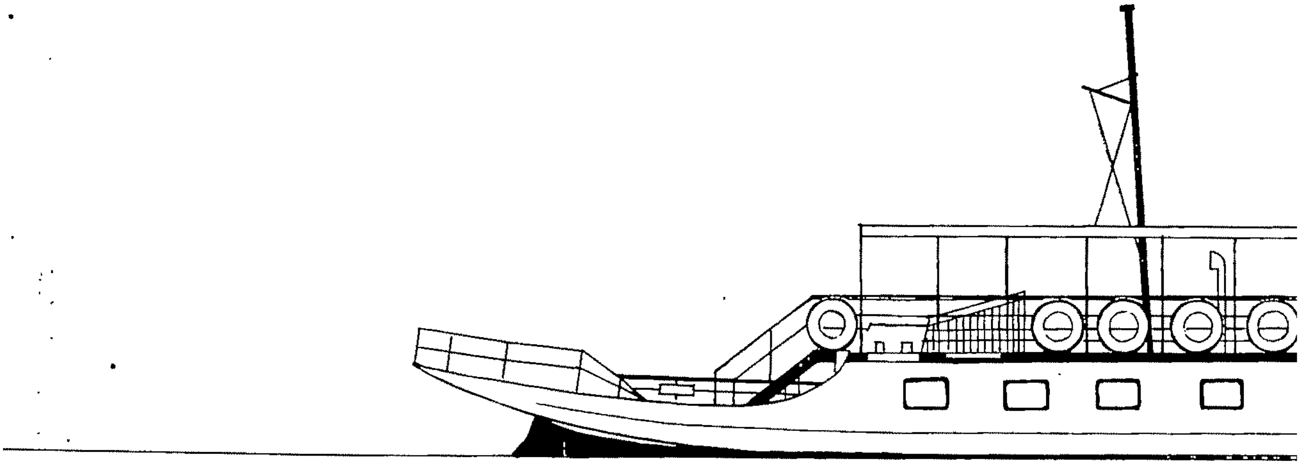
Annual Subscription: £10·00 (post free)

Single Numbers: £3·00 (post free)

JOHN WRIGHT

42–44 Triangle West, Bristol BS8 1EX

Missed it?

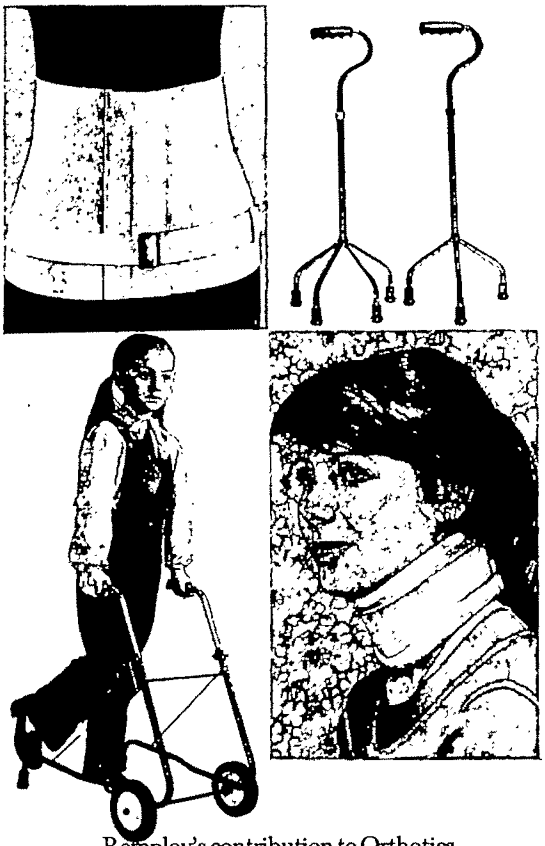


Aminoplex 5
Aminoplex 14
Aminutrin
Calonutrin
Nefranutrin

Geistlich Nutrition

Geistlich Sons Limited Chester

Our experience is something you can rely on



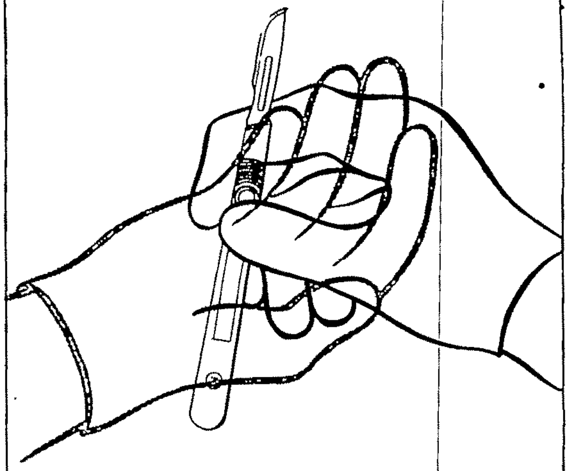
Remploy's contribution to Orthotics goes far beyond providing a comprehensive range of orthopaedic equipment.

Remploy are able to offer a unique measuring and fitting service for all their appliances and footwear, and have produced two orthopaedic brochures which are an invaluable aid to work in this field. Rely on this experience and send for literature, now.

Remploy

An exceptional name in Orthotics

A.H. Knight Remploy Limited (Orthopaedic Division),
Remploy House, 415 Edgware Road, Cricklewood,
London NW2 6LR. Telephone: 01-452 8020.



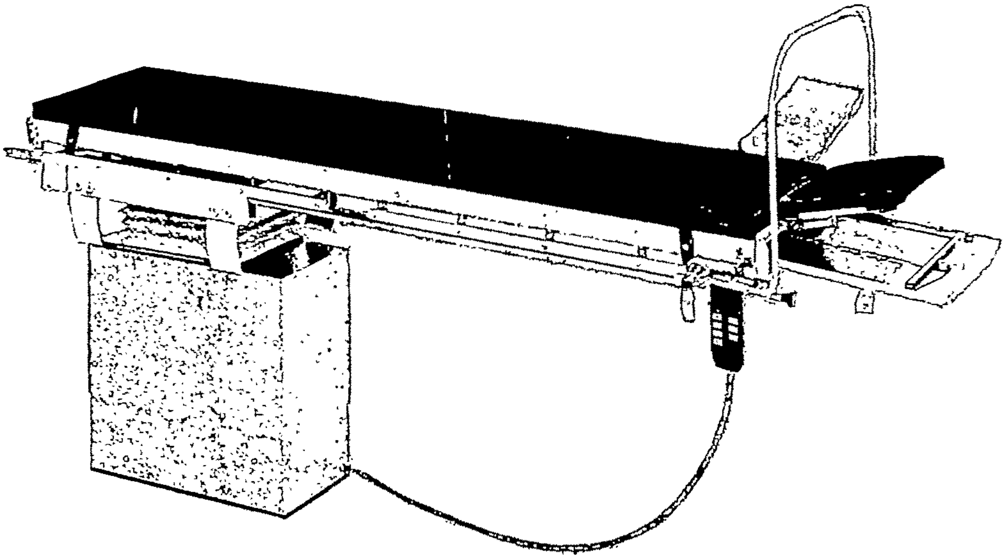
Another surgeon is about to use one of the world's finest surgical blades.... ...this happens thousands of times every day!

It happens because the blades are by Swann-Morton, the people who meet the highest requirements in surgical knives.
We need say very little about our superiority. The world's surgeons have proved it for us!

Swann-Morton

SWANN-MORTON LIMITED
PENN WORKS, OWLERTON GREEN
SHEFFIELD S6 2BJ. ENGLAND.

Just 4 bolts and a compressed air line



that's all it takes to install the KIFA H3 Table

- ★ The most advanced operating table system available
- ★ Reduces patient handling
- ★ Provides unequalled x-ray facilities ★ Easily cleaned
- ★ Utterly reliable ★ Quick turn-round of patients

Table tops available for general, urological, gynaecological, orthopaedic and micro-surgery. Sierex will be pleased to supply details on request.

Sierex

Sierex Limited
15/18 Clipstone Street, London, W1P 8AE, 01-580 2464
Branches in *Aberdeen, Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester and Reading.*
Agents in *Belfast, Newcastle and Newport.*

GU

NEW

DIATHERMY
FORCEPS,
SCISSORS &
SCALPEL HANDLES
COVERED
WITH
LONG-LIFE..

Insulast

- Developed for autoclaving
- ECONOMICAL · saves on repairs
- SAFER · crack resistant
- THINNER · better grip
- Universal cable fitting

When ordering new diathermy
instruments, or requiring old
instruments to be re-insulated,
always specify 'INSULAST'
only obtainable from;

The G.U. Manufacturing Co. Ltd.

28a, Devonshire Street, London, W1N 2AJ
Telephone; 01-935-2835.

The LOR-1A
APPARATUS

CHRONIC TONSILLITIS
successfully treated by ultrasonic therapy

Detailed information available from

V/O MEDEXPORT

31 Kakhovka, Moscow 113461, USSR. Telex 7247
Tel: 121-01-54

The LOR-1A apparatus produces mechanical vibrations of ultrasonic frequency which have a therapeutic effect on infected tonsils. Clinical tests have shown 75% success in patients treated. Advantages of the LOR-1A are its small dimensions and low weight (less than 5 kg) and its proven safety, reliability and ease of operation. Small ultrasonic generator of low operating voltage permits direct treatment to tonsils.

H. K. Lewis & Co. Ltd.

*Medical Publishers
and Booksellers*

136 GOWER STREET
LONDON, WCIE 6BS

Telephone : 01-387 4282

LEWIS'S MEDICAL LIBRARY

Annual Subscription from £4·00

Books may be exchanged as often as desired. There are reduced rates for multiple subscriptions.

Prospectus post free on request

ADVERTISEMENT RATES

Display	No. of issues 1–5	6–11	12
Whole page	**£80**	**£76**	**£72**
Half page	**£45**	**£43**	**£41**
Quarter page	**£25**	**£24**	**£23**

Special Positions	No. of issues 1–5	6–11	12
Outside back cover	**£130**	**£120**	**£110**
Inside front or back cover	**£100**	**£95**	**£90**
Facing matter or in text	**£95**	**£91**	**£87**

Colour Rates **£40** extra per colour. Full colour **£100** extra
Bleed Page **£10** extra
Loose Inserts Two-page **£80**. Four-page **£140**. Stitched-in by arrangement
Copy Date Two months preceding publication date

Advertisement Representatives:

HEXAGON PUBLISHING CO. LTD., 10 Spencer Street, St Albans, Herts AL3 5EG
Telephone: St Albans 60641

Charles Davis
1850-1920

Fred Geck
1856-1942

History shows that between them they made an important contribution to the improvement of catgut as a suture material. They didn't achieve the ideal, but then, their tradition was in catgut.

In 1962, the Davis and Geck research team started on a new approach, breaking with tradition. Their objective was to develop a better, natural, absorbable suture, because of the inherent unavoidable problems of catgut's basic material, animal intestines.

From this research came DEXON* sutures, formulated from the juice of grapes and other fruit. DEXON*, now proven to be the ideal natural absorbable suture.

If you are still using catgut, this could be the right time to consider a break with tradition. DEXON* sutures may take a little getting used to, but you, and your patients, will quickly see the advantages. However, if you prefer to stay with tradition, Davis and Geck catgut is still the best available.

Thanks to the years of research by Mr. Davis and Mr. Geck.

*Trademark

DG
DAVIS + GECK

A Division of Cyanamid of Great Britain Limited Fareham Road Gosport
Hampshire PO13 0AS Telephone Fareham (03292) 6131
A Tradition of Innovation

ACM endoscopes leave nothing to the imagination

ost surgeons today recognise the superiority of endoscopy as a ans of confirming diagnoses of colon diseases. It can be quicker d easier than laparotomy, and is also less traumatic for patients and kes fewer demands on hospital facilities.

The premier instrument for colonic investigations is the ACM F9L oscope. Advanced features include 12X magnification and a sharp, de angle circular image three times larger than competitive trument's.

With it a surgeon can clearly view as far as the caecum, take biopsy ecimens and perform polypectomies. After surprisingly little ctice, coloscopy can be most rewarding. And the ACM coloscope xceptionally easy to use – a single, one-handed joystick controls poly-directional tip.

There's a shorter version, too, the F9S which will reach to the nsverse colon and beyond. For the experienced coloscopist there's the dual channel F9A, a major operative, as well as diagnostic instrument.

To find out more, please use the coupon. Or write or telephone.

Please tell me more about ACM endoscopes
I would like literature only ☐
Please arrange a visit
My telephone number is ☐
Name
Address

B.J.S. 9.75

ACM

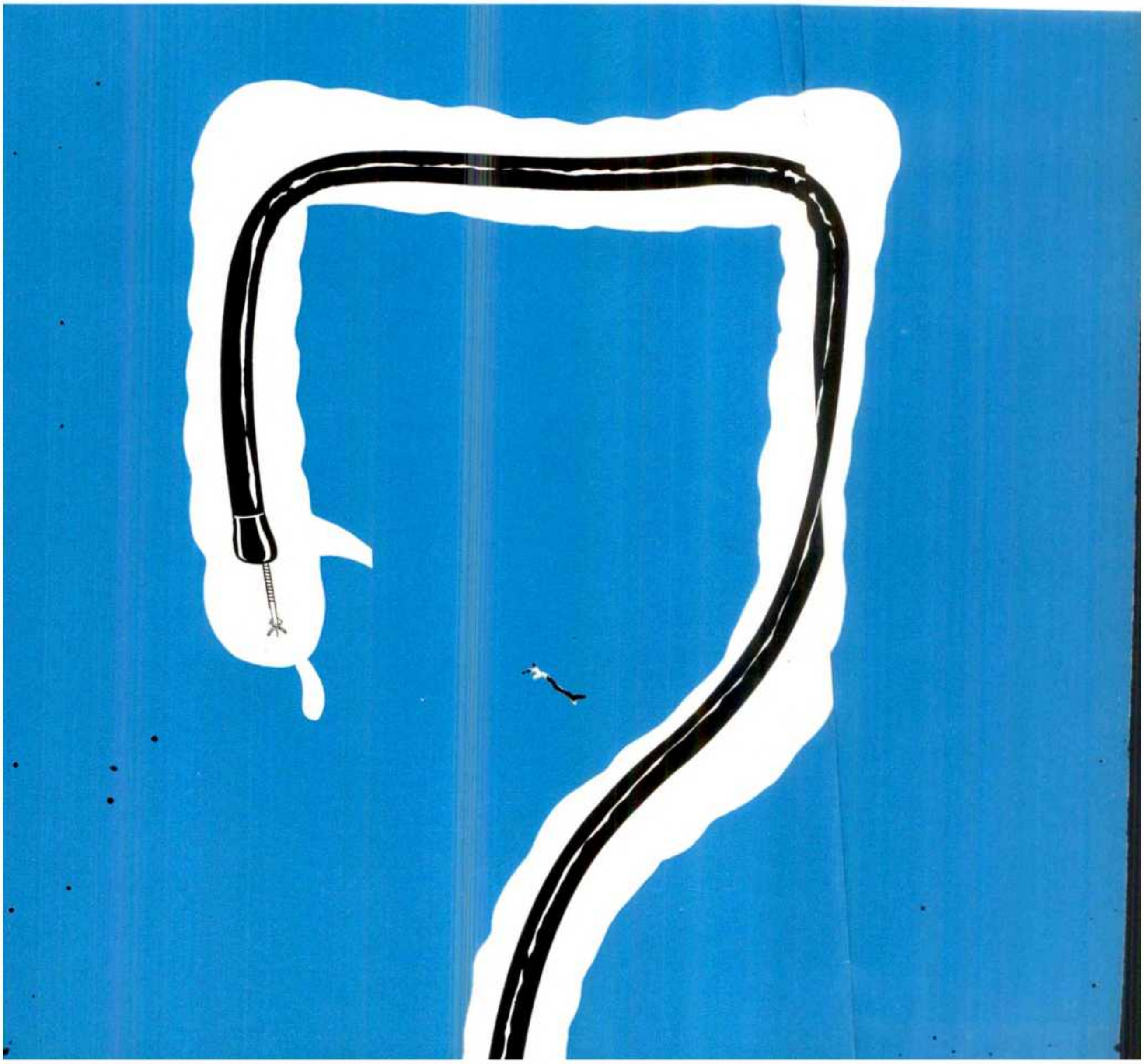
WAPPLER ENDOSCOPY LIMITED

Park House, 22 Park Street, Croydon, Surrey, CRO OYH
Telephone: 01-686 4241

WAPPLER Endoscopy Limited

ACM Endoscopes – clearly the best

ACM endoscopes for gastro-enterology, bronchoscopy, urology, gynaecology and teaching.



staphylocidalpenetrateability!

no other word
is big enough for
fucidin*

'This antibiotic has now established itself as an important antistaphylococcal agent in the eatment of systemic infection. Good absorption d minimal side effects after oral administration combined with an impressive penetration in deep-seated infections gives fucidin an important place in the management of staphylococcal infections.'

* fucidin is a trade mark for sodium fusidate

Further information available on request.

Leo Laboratories Limited,
Hayes Gate House, Hayes, Middx.

nted in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU

Trasylol

significantly reduces mortality and morbidity in acute pancreatitis

Trapnell, J. E. *et al.* (1974) *British Journal of Surgery*, **61**, 177.

Trasylol®

(aprotinin)

Bayer

® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

Vol. 62 : No. 12 : December 1975

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. O. ADESOLA Lagos : Nigeria
A. S. ALDIS Cardiff
M. ALLGÖWER Switzerland
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
S. BENGMARK Sweden
*A. B. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
SIR DONALD DOUGLAS Dundee
CHARLES DREW London
*H. A. F. DUDLEY London (Surgical Research Society)
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
TOM GIBSON Glasgow
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
E. HASNER Denmark
M. HOBSLEY London
E. S. R. HUGHES Melbourne : Australia
C. W. JAMIESON London
I. D. A. JOHNSTON Newcastle
SIR ANDREW W. KAY Glasgow
H. LARRIEU France
F. LINDER West Germany
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
A. C. McEACHERN Adelaide : Australia
L. D. MACLEAN Montreal : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
H. MULLER The Netherlands
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
G. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
L. SEMB Norway
ROBERT SHIELDS Liverpool
G. SLANEY Birmingham
D. SLOME London
G. SMITH Aberdeen
SIR RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
A. S. TILL Oxford
SURGEON VICE-ADMIRAL SIR JAMES WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX

Subscription £15 per annum, post free. Single copies £1·50, post free

THE WILLIAMS & WILKINS CO., BALTIMORE

Subscription $36·00 per annum. Single copies $3·00

Second Class Postage paid at Baltimore, and at additional mailing offices.

The new evidence for Trasylol in the treatment of acute pancreatitis

Prospective double-blind trial in 105 patients over a five year period shows Trasylol to significantly reduce mortality and morbidity in acute pancreatitis.[1]

Course of illness		
Mild	● 30 patients (56·6%)	○ 22 patients (42·3%)
moderate	● 13 patients (24·5%)	○ 9 patients (17·3%)
severe	● 6 patients (11·3%)	○ 8 patients (15·4%)
DIED	● 4 patients (7·5%)	○ 13 patients (25·0%)

● Trasylol group (53)
○ placebo group (52)

'Trasylol must therefore be regarded as a drug which is beneficial in the treatment of acute pancreatitis.'[1]

1 Trapnell, J.E. *et al.* (1974) *British Journal of Surgery*, **61**, 177

Trasylol®
(aprotinin)

Bayer
® Registered Trade Mark of Bayer Germany

Further information available from Bayer UK Limited,
Pharmaceutical Division,
Haywards Heath, West Sussex RH16 1TP

The British Journal of Surgery

Vol. 62: No. 12: December 1975

Original papers

		Page
Surgical complications of implanting pacemakers	Harold Siddons and K. Nowak	929
The efficiency of surgical masks of varying design and composition	Louis B. Quesnel	936
Identification of talc on surgeons' gloves and in tissue from starch granulomas	W. J. Henderson, C. Melville-Jones, W. T. Barr and K. Griffiths	941
The effect of metal clips on the tensile properties of healing skin wounds	I. D. Harrison, D. F. Williams and A. Cuschieri	945
How tight should tension sutures be tied? A controlled clinical trial	I. L. Rosenberg, T. G. Brennan and G. R. Giles	950
Does the choice of suture material affect the incidence of wound infection?	G. L. Mouzas and A. Yeadon	952
Gangrene of the tongue following self-application of a rubber band	T. Dutta and K. Vasudevan	956
In situ intraduct carcinoma of the breast: a long term follow-up study	R. R. Millis and G. S. J. Thynne	957
The survival rate of men with carcinoma of the breast	R. W. T. Slack	963
Operative cholangiography: a reappraisal based on a review of 400 cholangiograms	Irvin Faris, James P. S. Thomson, D. J. Grundy and L. P. Le Quesne	966
Carcinoma of the duodenum: its preoperative diagnosis	K. Satake, M. Sowa, K. Yamashita, K. Kamino, J. Kinoshita, M. Kato and K. Umeyama	973
Clinical features of the degenerate meniscus with the results of meniscectomy	Jonathan Noble	977
Pressure measurements beneath below-knee amputation stump bandages: elastic bandaging, the Puddifoot dressing and a pneumatic bandaging technique compared	P. A. Isherwood, J. C. Robertson and A. Rossi	982

Reviews and notices of books 987

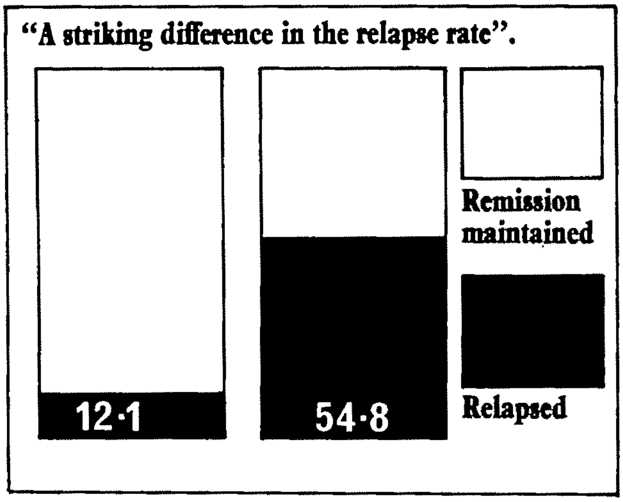
Index 990

© John Wright & Sons Ltd and the respective contributors named above, 1975.
All rights reserved. No part of this publication may be reproduced, stored in a retrievel system or transmitted in any other form or by any means electronic, mechanical, photocopying, recording or otherwise without prior permission of the copyright owner, for which application should be made to John Wright & Sons Ltd.

“It is concluded that maintenance treatment of ulcerative colitis with sulphasalazine (salazopyrin) should be continued indefinitely unless contraindicated by side effects”.[1]

The results of the above controlled trial carried out at the Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, are all the more welcome as earlier trials of cortisone[2] and prednisone[3] at standard dosages have shown them to be totally ineffective in reducing the number of recurrences of ulcerative colitis.

“Fortunately, Sulphasalazine tablets, 0.5 grams, 4 times a day will prevent relapses in the majority of patients with colitis, and only a few patients cannot tolerate this relatively small dose, which can be continued indefinitely, since we do not know when, if ever, it can be safely stopped”.[4]



“The patients who received dummy tablets had more than four times the relapse rate of those receiving sulphasalazine”.[1] (Salazopyrin).

Salazopyrin (sulphasalazine) is available as the plain 0.5 g. tablet, 0.5 g. EN-tab and as an 0.5 g. suppository. Literature and detailed information on Salazopyrin are available on request.

References
1. Gut (1973) 14 923–926
2. Brit. med. J. (1959) 1 387–394
3. Lancet (1965) i 188–189
4. General Practitioner (1972) April 7 p11.

Salazopyrin — to be continued indefinitely

Further information available from:—

Salazopyrin is a registered trade mark.

Pharmacia (Great Britain) Ltd.,
Paramount House,
75 Uxbridge Road,
London W5 5SS.
Telephone: 01-579 0102/7

Pharmacia

EDITORIAL NOTICES

Original articles or reviews are invited and editorial communications should be addressed to the *Editorial Secretary, British Journal of Surgery, c/o John Wright & Sons Ltd., Bristol BS8 1EX.* Articles are accepted on the understanding that they are contributed to this Journal only, and that articles and their illustrations become the property of the Journal unless the authors state, before publication, that they reserve the right to themselves. Each article should be accompanied by an adequate summary, suitable for publication. Authors are asked to ensure that original illustrations are securely packed and adequately protected.

BUSINESS COMMUNICATIONS should be addressed to *John Wright & Sons Ltd., British Journal of Surgery, Bristol BS8 1EX.* Remittances should be made payable to *The British Journal of Surgery.*

BINDING.—Handsome Cloth Cases may be obtained for binding Vol. 61. Case, £2·00 post free; Case and binding, £7·50 post free. Cases are also available for some of the earlier volumes. Applications should be made to the Publishers, who will also undertake the binding if desired.

ADVERTISEMENTS.—All communications should be addressed to *Hexagon Publishing Co. Ltd., 10 Spencer Street, St Albans, Herts AL3 5EG* (telephone St Albans 60641).

Instructions to Authors

PREPARATION OF MS.—Papers should be submitted in typescript and the author should retain a carbon copy. Double spacing should be used throughout, except for quotations.

ILLUSTRATIONS AND TABLES

Illustrations should be clearly marked on their backs to show number, orientation and author's name. Explanatory legends should be typed on a separate sheet of paper accompanying the manuscript. For halftones, glossy photographs or positive prints (*not* X-ray negatives or slides) should be sent, unmounted wherever possible. When coloured illustrations are submitted as colour prints, they should be accompanied by the original transparencies where possible. As colour illustrations are expensive to reproduce, authors may be asked to make a contribution towards the cost. Drawings should be in a finished state suitable for reproduction. Any lettering should be large enough to withstand a reduction in size; sans serif lettering is recommended. Leaflets giving further instructions are available on request.

Tables should be typed on separate sheets of paper accompanying the manuscript. They should have an identifying number and a short descriptive heading. *All illustrations and tables must be referred to in the text.*

PRESENTATION OF STATISTICS

Authors are reminded that with the frequent use of statistical analysis in biological writing of all kinds it is desirable that:

a. The methods section of a paper should contain a mention of any statistical technique used. If the method is new or unfamiliar either a reference should be given or a description included as a brief appendix.

b. If alternative techniques could have been applied to the data, a short justification of the method is often appropriate.

c. In clinical trials the confidence or tolerance limits of the results should be quoted, particularly when formal statistical significance at the 5 per cent level is only just reached.

d. Abbreviations for statistical terms should follow those used in *Documenta Geigy Scientific Tables*, 7th edition, 1970.

REFERENCES

The citation of references should follow the pattern shown in the Reference Citation Recommendations issued by the Medical Section of the Library Association. Copies of these recommendations can be obtained from the Secretary, Medical Section, The Library Association, 7 Ridgmount Street, London WC1E 7AE.

The name of the author and the date of publication are given in the text; the list of works cited is put at the end of the article, arranged in alphabetical order of authors' names. When references to two or more works by the same author are listed, they are arranged in chronological order. Where there are more than two authors these may be indicated in the text citation by the words 'et al.', following the name of the principal author; on the rare occasions when this may lead to confusion, the text citation should name as many of the collaborating authors as are necessary to identify the work cited. When several works published by the same author(s) in the same year are cited, they should be distinguished by the letters a, b, c, etc., placed immediately after the date.

In the list of works cited each reference to a *journal article* should give, in the order indicated, the names and initials of all authors, the year of publication (in parentheses), the title of the paper, the name of the journal (abbreviated), the volume number (in heavy type arabic numerals) and the numbers of the first and last pages of the article. Abbreviations for journal titles should be those adopted by *Index Medicus* since January 1971; where no abbreviation is given by *Index Medicus* the journal title should be left in full and the publishers will provide a suitable abbreviation. A reference to a *book* should give, in order, the names and initials of all authors, compilers or editors, the date of publication (in parentheses), the title of the book, the edition number (if other than first), the place of publication, the publisher's name and, where appropriate, the number(s) of the page(s) referred to. A reference to a *contribution to a book* should give, in order, the names and initials of all authors of the contribution, the date of publication (in parentheses) and the title of the contribution; then, after the word 'In:', there should follow the name(s) and initial(s) of the author(s) etc. of the book, the title of the book, the edition number (if other than first), the place of publication, the publisher's name and the numbers of the first and last pages of the contribution.

Titles of papers and books should be given in the original language, with titles in Cyrillic and Greek alphabets transliterated.

Only in papers in which many and frequent references have to be made should the items be numbered; the numbers may then be inserted in the text without interrupting it with a list of names and dates.

Examples

References to periodicals

BURKE D. C. (1961) The purification of interferon. *Biochem. J.* **78**, 536–563.

CRICK F. H. C. and WATSON J. D. (1956) Structure of small viruses. *Nature (Lond.)* **177**, 473–476.

In an anonymous paper where the name of the journal is used for quotation it is not repeated:

BRITISH MEDICAL JOURNAL (1969) Psychogenic dyspnoea **4**, 382.

For journals without volume numbers the page numbers are indicated by pp.

ISLIP P. J. and WHITE A. C. (1964) Some reactions of 2-(3-oxindolyd) ethylamines. *J. Chem. Soc.* pp. 1201–1204.

References to non-periodical literature

Books

PAZZINI B. (1941) *La Medicina Primitiva.* Milano, Arte e Storia.

DUBOS R. H. and HIRSCH J. G. (ed.) *Bacterial and Mycotic Infections of Man*, 4th 3d. London, Pitman Medical.

Contributions to books

PORTERFIELD J. S. (1963) Interference and interferon. In: HARRIS R. J. (ed.), *Techniques in Experimental Virology.* London, Academic Press, pp. 305–326.

Contributions to symposia

GRAY J. A. B. (1962) Coding in systems of primary receptor neurons. In: BLAMENT J. W. L. (ed.), *Biological Receptor Mechanism. Symposia of the Society for Experimental Biology*, no. 16. Cambridge, Cambridge University Press, pp. 345–354.

Congress Proceedings

CORNFORTH J. W., CORNFORTH R. H. and MATHEW K. K. (1959) A new stereo-selective synthesis of olefins and its application to the synthesis of all-trans-squalene. In: MOSETTIG E. (ed.), *Biochemistry of Steroids. Proceedings of the Fourth International Congress of Biochemistry, Vienna 1–6 September 1958*, vol. 4, pp. 59–60.

LOFTS B. (1965) Seasonal lipid changes and their possible significance in the testis of Anura. In: *Proceedings of the Second International Congress of Endocrinology, London, 17–22 August 1964.* Amsterdam, Excerpta Medica, pp. 100–105. (*Excerpta Med. Int. Congr. Ser.* 83.)

Series details should be included when they assist in identification of the reference, as in the example preceding, or that following.

SAINSBURY P. (1955) *Suicide in London.* London, Chapman & Hall. (Maudsley Monograph No. 1.)

eptrin b.d. in otitis media

etter for him better for mum

Better for him because Septrin has a powerful activity against the causative pathogens ensuring a rapid response and high success rates.[1,2]

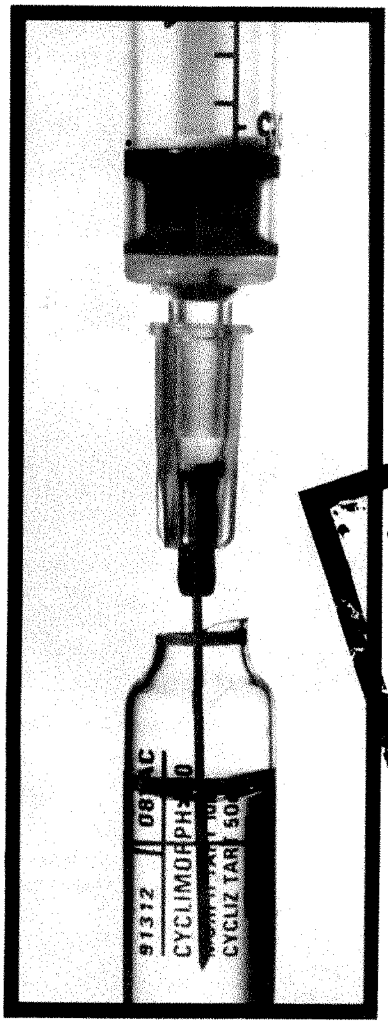
Better for mum because the twice-daily dosage of Septrin removes the worry of giving medicine at awkward times of the day and night.

1 *J infect Dis,*(1973), **128**, suppl, 629. 2 *Canad med Ass J,*(1975), **112**, 87S.

Septrin contains trimethoprim and sulphamethoxazole.
FULL PRESCRIBING INFORMATION IS AVAILABLE ON REQUEST.
Wellcome Medical Division, The Wellcome Foundation Ltd., Berkhamsted, Herts

llcome

SEPTRIN



NOW
MORPHINE
MINUS
VOMITING

CYCLIMORPH

TRADE MARK

CYCLIMORPH Injection has all the benefits of morphine plus an effective anti-emetic, cyclizine – in a single injection.

Cyclizine significantly reduces the incidence of nausea and vomiting,[1] whether associated with the condition or morphine-induced.

CYCLIMORPH is indicated in all conditions where morphine is needed.

[1] *Br. J. clin. Pharmac.* (1975), 2, 81.

Full prescribing information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd.
Berkhamsted, Herts

The British Journal of Surgery

Vol. 62 : No. 12 : December 1975

Br. J. Surg. Vol. 62 (1975) 929–935

Surgical complications of implanting pacemakers

HAROLD SIDDONS AND K. NOWAK*

SUMMARY

An analysis of the complications of implanting pacemakers at St George's Hospital between 1967 and 1973 highlights the difficulties of implanting foreign bodies. During this 7 years 1543 pacemakers were implanted in 779 adults. In 91 patients there were 118 implants with surgical complications, most of them due to a pressure necrosis or local infection; 3 septicaemias occurred. The various complications are classified and related to technique of implantation. Methods of management of the complications are presented.

As an Appendix the operative techniques of first and subsequent implantations are outlined.

THROUGHOUT the period of study endocardial (transvenous) electrodes have been used as the first method of pacing. Only 41 of the implantations have been with epicardial electrodes. Most of the pacemakers have been the British-made Devices models, but a few products of eight other manufacturers have also been used. The average life of the Devices pacemakers was between 2 and 3 years.

The optimum technique of implantation has been developed over the 7 years, and skin necrosis over the implant has been attributed in many instances to failure to comply with basic surgical principles, the importance of which became evident as experience grew. Operative procedure as now recommended is described in the Appendix.

The site most frequently chosen was the lateral chest wall behind the pectoral fold, referred to throughout this paper as the axilla, but the anterior chest wall was also used, particularly in women. When using electrodes placed on the heart at operation the pacemaker was put behind the rectus in its sheath, and this site was occasionally used with endocardial electrodes.

Owing to the possible risk of ventricular fibrillation, when an endocardial wire provides a low impedance path to the heart, diathermy has not been used in this series. Some of the patients have been on anticoagulant therapy; there has not been undue bleeding when the prothrombin time has not been excessive. The pacemaker pockets have not been drained.

Classification of complications

Of the 1543 implantations, 118 (7·6 per cent) required some form of revision due to wound complications. (The minimum period of follow-up was 12 months.) These complications can be divided (*Table I*) into: (1) a group of 39 which appeared to be inflammatory, (2) a group of 64 in which the pacemaker or electrode produced skin necrosis and (3) 15 miscellaneous complications.

Table I: CLASSIFICATION OF SURGICAL COMPLICATIONS

Group	No. of complications	Total	% of 1543 implantations
1. Inflammatory		39	2·5
Wound infection			
'Early'	25		
'Sinus'	11		
Septicaemia	3		
2. Skin necrosis		64	4·1
Over pacemaker	52		
Over wire	12		
3. Miscellaneous		15	1·0
Pain	5		
Wound dehiscence	5		
Pacemaker rotation	2		
Haematoma	2		
Muscle twitch	1		
Total		118	7·6

Group 1

These patients presented in three different ways: (*a*) with the signs and symptoms characteristic of inflammation ('early', 25 cases); (*b*) by developing a sinus in the scar ('sinus', 11 cases) and (*c*) with septicaemia (3 cases). The time elapsing between implantation and revision is shown in *Fig.* 1.

The 25 patients with signs of inflammation are considered to have been contaminated with bacteria at the time of operation. Infection was evident within 4 weeks in 17 cases. In 8 the implant did not require surgical attention for between 1 and 6 months.

---

* St George's Hospital, London.

LIBRARY

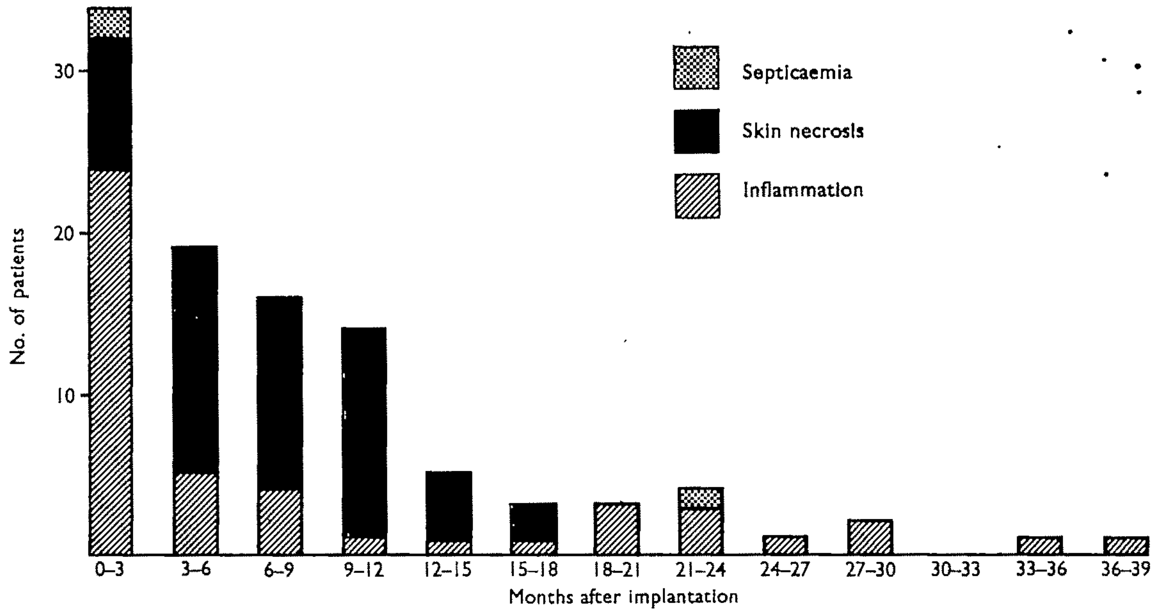


Fig. 1. Period between implantation and revision.

Wound cultures were rarely taken before the skin barrier had been broken by discharge. Early swabs were nearly always sterile, and the use of antibiotics may account for this. After a few days the commonest organism grown was *Staphylococcus albus*. Although this may have been a contaminant there is some evidence that in the presence of a foreign body it may be a significant organism (Wilson and Stuart, 1965).

The sinus with which 11 patients presented was always in the scar. This distinguished them from the 64 patients in group 2 in whom the skin gave way over the most prominent part of the pacemaker or wire. It is not certain that this type of reaction was due to a bacterial infection. In the few in whom fluid was obtained from the pacemaker pocket before a sinus to the surface had allowed bacteria to enter, the exudate was sterile. It is possible that the reaction was to the material covering the pacemaker, though it was not confined to any particular covering material.

It is instructive to relate the percentage of cases showing inflammatory complications (subgroups 1*a* and *b*) to the surgical facilities available at the time of implantation. Throughout the series all the operations for placing electrodes on the heart surface have been done in the operating theatre. However, for the first 21 months of the period surveyed the operations involving placing endocardial electrodes were carried out under the image intensifier in the X-ray department which was not specially designed for sterile procedures. For the remaining 5½ years the procedures were carried out in a specially designed small operating room. The percentage of inflammatory complications (both early and late) before the change was 3·7 per cent (7 of 190) and after the change 2·3 per cent (31 of 1353). These figures do not show a statistically significant difference.

The use of the operating room can be divided into two periods. At first all the procedures were covered with prophylactic ampicillin 1 g daily and cloxacillin 1 g daily for 5 days. Later, for a period of 18 months antibiotic cover was only used if there was a special indication, such as previous infection, operative contamination or diabetes. In this period antibiotics were used in less than 5 per cent of all cases. The rate of inflammatory complications when using the operating room with antibiotic cover for all patients was 2·8 per cent (25 of 890), and since reducing the use of antibiotics to only in a few selected cases it was 1·3 per cent (6 of 463).

The incidence of inflammatory complications in subgroups 1*a* and *b* has clearly been linked with repeated operations at the same site, and almost half (17 of 36) the inflammatory incidents had been preceded by wound infection or skin necrosis with previous implants. The incidence of these complications following 726 first implantations was 5·4 per cent and following 817 subsequent implantations 7·5 per cent.

Two other factors appeared to influence the incidence of wound inflammation: the use of epicardial electrodes and the abdominal site for pacemaker implantation (*Table II*). The comparisons are not strictly valid as the epicardial electrodes were used almost exclusively in patients who had previously been paced endocardially and had developed complications such as repeated electrode displacement or a rise in the endocardial threshold required for effective pacing.

There was no significant difference in the incidence of skin necrosis in those with axillary-sited pacemakers (39 ulcerated in 1130 = 3·5 per cent) compared with those with pacemakers sited anteriorly (8 ulcerated in 326 = 4·1 per cent).

The 3 patients in group 1*c* developed septicaemia. In 2 there was a clear explanation of the cause. In one of them a small abscess developed at the vein entry

Table II: COMPLICATIONS RELATED TO ELECTRODE AND IMPLANT SITE

Electrode and pacemaker site	No. of implants	Inflamed	Skin necrosis	Other	Total complications
Endocardial					
Chest wall	1447	27	56	13	96
Abdominal wall	53	6	5	0	11
Epicardial					
Chest wall	9	1	0	0	1
Abdominal wall	34	5	3	2	10
Total	1543	39	64	15	118

site in the neck, and the septicaemia was evident within 18 days of implantation. The second patient had had prolonged treatment with the electrode wire coming through the skin to an external pacemaker before implantation. The third patient was found at autopsy to have undiagnosed aortic stenosis with vegetations on the valve. The implant had been in place for nearly 2 years. Ten blood cultures during his terminal pyrexial illness were negative, but *Staph. albus* and α-haemolytic streptococcus (viridans type) were grown from the valve vegetations. The incident is recorded for completeness, but it is believed that the septicaemia was not related to the pacemaker system.

Group 2

More common than the inflammatory reaction to bacterial contamination or the chemical nature of the pacemaker is its *mechanical* effect. Pressure necrosis of the overlying tissue and eventually of the skin has proved a serious problem. There is usually no difficulty in determining that the skin is giving way as a result of a mechanical effect rather than an inflammatory reaction. Over a period of weeks the tissue covering the pacemaker thins, takes on a dusky red hue and then necroses. Once the skin has given way, bacterial invasion complicates the picture, though gross suppuration may not follow for weeks or months. The site of the lesion is over the most prominent part of the pacemaker and rarely at the site of the incision, which is invariably the site with inflammatory sinuses.

Such mechanical necrosis developed in 64 of the 1543 implantations. In many of these it was possible to forestall bacterial infection by resiting the pacemaker before the skin had completely given way.

Group 3

These 15 miscellaneous cases consist of: 5 in which pain over the pacemaker necessitated resiting; 5 in whom a wound dehiscence occurred, possibly as a result of taking out the sutures too soon; 2 with haematomas which were so large that they necessitated evacuation; 2 in whom the patient rotated the pacemaker, pulling on the electrodes and endangering their position; 1 with twitching due to local muscle stimulation.

Management of complications

Haematomas and other effusions

These have only been aspirated if they threatened to disrupt the suture line and discharge. Even if aspiration is expertly performed, there is a subsequent tendency for fluid to seep out and this may lead to ascending infection. If infection is thought to be the cause of a pocket effusion, aspiration is indicated.

Infection

At the first sign of infection a combination of an antibiotic suitable for prevalent staphylococci and a wider spectrum antibiotic was given systemically. A few infective incidents subsided with this régime. Once purulent material, whether sterile on culture or not, was draining, this treatment proved disappointing. Temporary improvement was almost always followed later by a discharging sinus, even with prolonged antibiotic treatment. Early in our experience it became clear that the prolonged treatment could be avoided if it was accepted at an early stage that the pacemaker should be removed and a new pacemaker implanted at a new site. The electrode was chemically sterilized *in situ* and reused, without recurrence of infection in 8 of 10 cases. At operation care was taken to separate the new from the old site, which was drained for 24 hours. Perhaps the safest method is to use a new electrode on the contralateral side, though even this has been followed by infection on occasion.

In patients with grossly infected wounds the pacemaker was taken out, the wire arranged so that it had a long subcutaneous track before entering the vein and pacing was continued with an external pacemaker until the suppuration had subsided. Thorough attempts were made to clear the skin of pathogenic bacteria by repeated skin preparation before implanting an alternative pacing system.

Septicaemia

In both the patients in whom septicaemia was diagnosed the infection was controlled by antibiotics. The original electrodes were changed for others using different veins. This proved satisfactory in one, but septicaemia recurred in the other who was then paced with an epicardial electrode. The third patient was not under our care for his terminal illness. Septicaemia was not diagnosed until after death.

Skin necrosis

Provided that the skin had not completely given way and there was no infection, the pacemaker or a replacement was reimplanted in a new site, taking all possible steps to provide adequate soft tissue cover. If the pouch had been made too superficial the new site was prepared deep to the walls of the old pouch, which themselves provided a good layer of protective tissue interposed between the outer surface of the pacemaker and the skin. Sutures were used to separate the new pouch from the old pocket, which was drained for 24 hours through a separate stab incision. Sometimes when the wire protruded it was possible to reroute it along a deeper course. Occasionally, silk fixation stitches appeared to be the cause of a sinus and removal of the stitch with little other revision resulted in prompt and permanent healing.

Discussion

The *incidence* of surgical complications is similar in this series to that reported by others. However, few of these reports have related the complication rate to technique, and the length and completeness of follow-up are not always indicated.

Analysing the figures from 21 authors (Edhag and Lagergren, 1969; Witte et al., 1969; Fishman et al., 1970; Goldman et al., 1970; Seling and Sykosch, 1970; Shepard et al., 1971; Dixon et al., 1972; Imparato and Kim, 1972; Conklin et al., 1973; Homan van der Heide et al., 1973; Kantrowicz et al., 1973; Linschoten et al., 1973; McLaughlin et al., 1973; Mascarenhas and Center, 1973; Seremetis et al., 1973; Torresani et al., 1973; Codini et al., 1974; Sowton et al., 1974; Uhrenholdt et al., 1974; Williams et al., 1974), each of whom have reported 100–800 implantations in the past 5 years, the mean figure for surgical complications is 5·1 per cent in 7205 implants. (This incidence may be an underestimate as not all the reports indicated whether they included skin necrosis with infection.) The lowest infection rates were recorded by Linschoten et al. (1973), with 277 primary implants using endocardial electrodes without infection and only 2 infections in 308 replacements, and by Conklin et al. (1973) with 2 in 403 implantations.

In the present series the overall *inflammation* incidence (excluding skin necrosis) was 2·5 per cent and with the technique currently used 1·3 per cent. These figures, which certainly show no greater infection rate without antibiotics, justify the policy of not using prophylactic antibiotics routinely. If antibiotics do confer a significant reduction of the infection rate this series is probably large enough to have shown it. The practical disadvantages of incurring the risk of drug sensitivity reactions must be considered. In the period when cloxacillin and ampicillin were used routinely diarrhoea and other intestinal symptoms were more common than without them. Hospital discharge frequently had to be delayed for this reason.

The results of this series also indicate that haematoma formation with its added risk of infection can be kept at an acceptable rate without draining the pacemaker pocket or using diathermy.

The incidence of *skin necrosis* in the present series of 4·1 per cent is much more disturbing and an analysis has been carried out to see if the records clearly relate skin necrosis to any particular step in technique. It was concluded that details of technique are of relevance and that often subsequent skin ulceration could be attributed to failure to adhere to basic surgical principles. The implantations in this series were done by a large number of surgeons and physicians of differing experience. Moreover, the importance of some points in technique, particularly when reimplanting after previous complications, was not appreciated early in the series. The results relate not specifically to the technique recommended, but to the methods whilst details of technique were being evolved.

Skin necrosis is more common in thin (and elderly) patients but occurs also when the subcutaneous tissues are lax and the pacemaker does not become firmly fixed. The incidence of this complication depends on the shape, size and weight of the pacemaker, and also on the site of implantation. Over the past 14 years manufacturers have done much to improve pacemakers by rounding off sharp corners, but they remain large and heavy foreign bodies. In 12 of the 64 skin necrosis incidents it was the wire and not the pacemaker which protruded. Early in this series the vein most often used was the external jugular, and occasionally erosion of the wire to the skin surface in the neck resulted. The use of the deeper cephalic vein has reduced the incidence of wire ulceration, but it can occur when a loop of wire is left close to the surface.

Parsonnet (1972) has stated that skin necrosis is ten times as common following reimplantations than following the initial implant. Homan van der Heide et al. (1973) reported an incidence of infection of 2·2 per cent of 268 first implantations and 6·0 per cent of 547 subsequent implantations. The figures of Kennelly et al. (1974) are 1 per cent of 196 first implantations and 4 per cent of 204 subsequent implantations. The figures reported here for infection and skin necrosis are 5·4 per cent of 726 first implantations and 7·5 per cent of 817 subsequent implantations.

Septicaemia is a recognized risk of long term intravenous pacing if the electrode traverses the skin barrier to an external pacemaker. With implanted pacemakers the risk of skin organisms travelling along the wire track to the bloodstream is eliminated. In 2 patients there was an obvious explanation for bloodstream bacterial invasion. The third patient had aortic valve disease and the bacterial endocarditis did not appear to be related to pacing.

It is interesting to note that a high rate of septicaemia (4 in 260) was recorded by Edhag and Lagergren (1969) when using a technique which involved leaving the pacemaker outside the body for a few weeks before implantation.

Twenty-one patients with septicaemia have been reported in the literature. In at least 6 of these there was local sepsis at the implant site or skin erosion (Imparato and Kim, 1972; Seremetis et al., 1973; Jablonka et al., 1974; Sedeghat, 1974). In others the only lesions to explain bacteraemia were a paronychia (Codini et al., 1974), a chest infection 2½ months after implantation (Waisser et al., 1972) and a sacral decubitus ulcer (Schwartz and Pervez, 1971). In the remainder clinical details on this point were not given (Bergovich and Fenig, 1970; Fishman et al., 1970; Torresani et al., 1973; Radford and Julian, 1974).

An analysis of a number of reports on the *management* of *infected pacemaker* pockets shows that treatment with parenteral antibiotics will not usually sterilize the pocket without resiting the pacemaker (Firor et al., 1968; Fishman et al., 1970; Seling and Sykosch, 1970; Dixon et al., 1972; Furman et al., 1973; Linschoten et al., 1973; Codini et al., 1974). If the pacemaker is not to be moved the most successful treatment appears to be frequent local irrigation with neomycin or kanamycin. Furman et al. (1973) reported success in 9 out of 13 infected pockets treated in this way. The present authors have also had success with this method, but find that it is quicker to make a new pocket, using a new electrode if there is heavy contamination.

Appendix

Procedure for pacemaker implantation

Pacemaker site: It is assumed that the electrode has been satisfactorily placed using the cephalic vein or, alternatively, a jugular vein. The axilla is the best site for the pacemaker. It may, however, prove unsuitable in very thin patients, particularly when there is no laxity or freedom of movement of skin over the ribs. It is also unsuitable if a particularly thick pacemaker is to be used and in relatively small patients. If the pacemaker is placed very high in the axilla it interferes with arm function and is uncomfortable, but most pacemakers lie comfortably a little lower behind the pectoral fold. (The Devices pacemakers which are 25 mm thick are not too large for this site in most patients. Lithium-celled units are considerably thinner.)

The next choice of site is on the pectoral muscle anteriorly, which is the position used most frequently in the USA. Cosmetically, this site is unsatisfactory in men, but in women the implant is hidden behind the breast. The pacemaker should be implanted deep to the fascia ensheathing the pectoralis major. If it is placed outside this fascia skin necrosis is liable to occur, even in women with ample space behind the breast, as the pacemaker may move in the lax tissues. Some men have had pacemakers placed both low in the axilla and on the anterior chest wall on separate occasions. A large proportion of these men find the axillary site more comfortable.

With epicardial electrodes the abdominal wall is the most convenient implant site. Pacemakers placed within the rectus sheath behind the rectus are stable and well protected, but their depth necessitates a more disturbing operation when they are replaced. If they are placed subcutaneously they require fixation to the deeper layer to prevent migration.

The side to be chosen is determined by the preference for placing the transvenous electrode. The majority in this series have been right-sided.

Preparation: The patient lies prone on a sterile drape covering a plastic foam sheet with a single pillow for the head which is turned away from the site of operation. The elbow is placed a few inches from the side so that the arm forms a triangle with the chest wall, giving good access to the axilla. Great care must be taken to keep the surgical drapes in place. The area is irregular in shape and so is unsuitable for adhesive plastic covers.

Anaesthesia: Local anaesthesia is preferred in psychologically suitable patients, and hospital stay is minimized by avoiding a general anaesthetic.

The incision: The incision used for introducing the electrode into the cephalic vein should not be extended downwards for the pacemaker's implantation as it is too remote from the best pocket site and vertical incisions in this area give puckered scars. A separate horizontal incision over the anterior aspect of the pectoralis major is preferred. This muscle is retracted medially and a pocket developed behind it on the lateral chest wall between the pectoralis major and the latissimus dorsi.

This incision allows comfortable access to the preselected pacemaker site, and makes the creation of the correct-sized pocket easy; bleeding vessels are easily detectable and the pacemaker can be accurately placed behind the pectoral fold. Some authors advocate a single incision for both electrode and pacemaker implantation. With the implant site advocated here a single incision would not offer the advantages mentioned above.

Depth and size of the pocket: It is essential that the pocket be made close to the muscle so that as much fascia and subcutaneous tissue as possible lies between the pacemaker and the skin. The pocket is developed by blunt dissection with the fingers or the back of the blades of scissors. By this means the correct anatomical plane is not transgressed and there is minimal bleeding. Too big a pocket can allow the pacemaker to rotate, which can twist the electrode wire, damaging it, and even avulse it from contact within the ventricle.

Haemostasis: All bleeding points are tied with catgut. There is some risk in the use of diathermy when an electrode has been placed in contact with the ventricular endocardium, as it provides a low resistance electrical pathway to the heart and could produce ventricular fibrillation. Prolonged swab pressure controls the tiny bleeding vessels, which in other circumstances would be coagulated with diathermy. For this reason the pocket is made early in the operation and packed with swabs whilst the pacemaker is attached to the electrode.

Measuring threshold and R wave amplitude: The technique of attaching the electrode wire to the pacemaker varies with each pacemaker model and instructions are issued with the instrument. The threshold required to pace is checked immediately before the attachment is made. This is done by connecting two sterilized wires from a separate portable pacemaker with voltage (or amperage) control. The peak-to-peak QRS is also measured using the electrode as an intracardiac ECG lead. It is not necessary to measure impedance.

Placing the pacemaker: In placing the pacemaker, attention must be paid to the site of any protuberance such as the terminal of the electrode. This is best situated behind the lateral fold of the pectoral muscle to protect it from the skin. In individuals in whom subcutaneous tissue is either very sparse or very lax there may be less risk of skin necrosis if the pacemaker is enclosed in a Dacron mesh bag as described by Parsonnet (1972).

Pacemakers with one metal surface as the indifferent electrode must be put in with this surface turned away from muscle or twitching may result. (If the operation is performed under general anaesthesia with relaxants, such twitching may be obscured.)

Spare wire should be placed deep to the pacemaker where it is out of the way of subsequent incisions to change the pacemaker. If the pocket is not firmly closed with soft tissue the wire tends to spring out and may erode through the skin.

Wound closure: The pectoralis major muscle, when released from retraction, forms a good barrier between the implant and the incision. Good soft tissue closure is essential, providing a barrier between the foreign body and the skin. The interrupted skin sutures are removed when healing is seen to be firm and not on any specific day. Healing in elderly patients requiring pacemakers may be very slow, and wounds may break down after removal of stitches even if this is delayed for more than a week.

Drainage: Drainage of pacemaker pockets is not advised on the grounds that even if the drain is small and is removed within 24 hours the track may allow skin bacteria to enter the implant pocket.

Antibiotics: Prophylactic antibiotics are not used routinely. However, patients at special risk are treated with ampicillin 250 mg q.i.d. and flucloxacillin 250 mg q.i.d. by mouth, starting before operation and continuing for at least 5 days. Previous implant sepsis, any potentially septic skin lesion, phlebitis from an intravenous arm electrode or catheters, excessive bleeding and diabetes have all been regarded as indications for the use of antibiotics.

Procedure for changing the pacemaker

This operation, though very simple in principle, can be technically tedious and time-consuming. In the hands of the impatient or unskilled the insulation on the electrode can be easily damaged, and adequate soft tissue closure between the implant and the skin may not always be achieved.

Local anaesthesia is used, and provided that the previous incision has been properly placed and is not overlying the pacemaker, it is used again, excising the scar. A preoperative X-ray to show the course of the wire is valuable, and before cutting tissue in the vicinity of the wire careful fingertip palpation is essential. An opening movement of scissors is useful in exposing the wire without damaging it. The initial aim is to cut down on to the upper surface of the pacemaker and then to open the capsule over the upper surface sufficiently to be able to squeeze or hook the pacemaker out. In order to achieve this it is often necessary to enlarge the pocket. Incisions of the capsule for this purpose must be made on its deep surface to avoid the possibility of thinning the layer of tissue between implant and skin.

The method of disconnecting and reconnecting to a replacement pacemaker differs with various pacemaker models and is described by the manufacturers in pamphlets supplied with the instruments. It is important to measure the threshold required for pacing at each change of unit. Care must be taken not to pull on the electrode; it has occasionally been displaced from contact with the right ventricle in this way. Closure of soft tissue between the implant and the skin incision is as important with each change of pacemaker as with the initial implant.

References

BERGOVICH J. and FENIG S. (1970) Complications with permanent transvenous pacemakers. *NY State J. Med.* **70**, 761–766.

CODINI M. A., CARALIS D. G. and VOIGT G. C. (1974) Permanent ventricular pacing: a ten year experience. Complications of implantation, incidence of congestive heart failure and coronary artery disease. *Johns Hopkins Med. J.* **134**, 118–127.

CONKLIN E. F., GIANELLI S., AYRES P. M., MUELLER H. S. and GRACE W. J. (1973) Prevention of pacemaker infections. *NY State J. Med.* **73**, 2675–2677.

DIXON S. H., PERRYMAN R. A., MORRIS J. J. and YOUNG W. G. (1972) Transmediastinal permanent ventricular pacing. *Ann. Thorac. Surg.* **14**, 206–213.

EDHAG O. and LAGERGREN H. (1969) Transvenous electrodes. *Ann. NY Acad. Sci.* **167**, 761–768.

FIROR W. B., LOPEZ J. F., NANSON E. M. and MORI M. (1968) Clinical management of the infected pacemaker. *Ann. Thorac. Surg.* **6**, 431–436.

FISHMAN N. H., HUTCHINSON J. C., EDMUNDS L. H. and ROE B. B. (1970) Permanent transvenous pacemaker for senile heart block. *Am. J. Surg.* **120**, 187–191.

FURMAN S., ESCHER D. J. W. and PARKER B. (1973) Results of long-term pacemaker implantation. In: DREIFUS L. S. and LIKOFF W. (ed.) *Cardiac Arrhythmias.* New York, Grune & Stratton, pp. 599–605.

GOLDMAN B. S., BLACK L. L. and LIPTON I. H. (1970) Implantable transvenous cardiac pacemakers: indications, complications and management. *J. Am. Geriatr. Soc.* **18**, 905–915.

HOMAN VAN DER HEIDE J. M., BOSMA G. J., KLEINE J. W., THALEN H. J. TH., NEIVEEN J. and BARTSTRA M. (1973) Results with pacemaker implantations. In: THALEN H. J. (ed.) *Cardiac Pacing.* Assen, The Netherlands, Van Gorcum, pp. 253–267.

IMPARATO A. M. and KIM G. E. (1972) Electrode complications in patients with permanent cardiac pacemakers. *Surgery* **105**, 705–710.

JABLONKA S., WIDOMSKA-CZEKAJSKA T., WILGOSZYNSKI A., MODRZEWSKI Z., KURYECIO L., BIELAK J., MOZIARA Z. and TOMASZEK M. (1974) Problemy chirurgiczne zwiazane ze stosowaniem elektrycznej stymulacji serca. *Pol. Tyg. Lek.* **29**, 839–841.

KANTROWICZ A., RUBENFINE M. and WAJSCZUK W. (1973) Complications of permanent transvenous pacemaker therapy. In: THALEN H. J. (ed.) *Cardiac Pacing*. Assen, The Netherlands, Van Gorcum, pp. 244–252.

KENNELLY B. M. and PILLER L. W. (1974) Management of infected transvenous permanent pacemakers. *Br. Heart J.* **36**, 1133–1140.

LINSCHOTEN H., MEIJNE N. G., MELLINK H. M. and OVERDIJK A. D. (1973) Pacemaker implantation and infection. *J. Cardiovasc. Surg.* **14**, 126–130.

MCLAUGHLIN J. S., COHEN M. L., SINGLETON R., ATTAR S., SCHERLISH L. and COWLEY A. (1973) Permanent transvenous catheter pacing: six year experience. *J. Thorac. Cardiovasc. Surg.* **66**, 771–777.

MASCARENHAS E. and CENTER S. (1973) Results of permanent pacemaker therapy. In: SAMET E. (ed.) *Cardiac Pacing*. New York, Grune & Stratton, pp. 175–200.

PARSONNET V. (1972) Critical review: power sources for implantable cardiac pacemakers. *Chest* **61**, 166–173.

RADFORD D. J. and JULIAN D. G. (1974) Sick sinus syndrome: experience of a cardiac pacemaker clinic. *Br. Med. J.* **3**, 504–507.

SCHWARTZ I. S. and PERVEZ N. (1971) Bacterial endocarditis associated with a permanent transvenous cardiac pacemaker. *JAMA* **218**, 736–737.

SEDEGHAT A. (1974) Permanent transvenous pacemaker infection with septicaemia. *NY State J. Med.* **74**, 868–869.

SELING A. and SYKOSCH H. J. (1970) Pacemaker und infektion. *Thoraxchirurgie* **18**, 336–345.

SEREMETIS M. G., DE GUZMAN V. C., LYONS W. S. and PEABODY J. W. (1973) Cardiac pacemakers: clinical experience with 289 patients. *Am. Heart J.* **85**, 739–748.

SHEPARD R. B., VAUGHN E. and REDMOND S. (1971) Cardiac pacemaker experience, 1961–1970. *Am. Surg.* **37**, 691–699.

SOWTON E., HENDRIX G. and ROY P. (1974) Ten-year survey of treatment with implanted cardiac pacemaker. *Br. Med. J.* **3**, 155–160.

TORRESANI J., JAUSSERAN J. M., BERNARD J., HOUVE A. and HENRY E. (1973) Advantages of permanent endocardial pacing: surgical technique and results. *J. Cardiovasc. Surg.* **14**, 535–541.

UHRENHOLDT A., HAGHFELT T., HANSEN J. F., LETH A. and MEIBOM J. (1974) Pacemaker treatment. Implanted pacemakers, function time, and complications. *Dan. Med. Bull.* **21**, 151–157.

WAISSER E., KUO C.-S. and KABINS S. A. (1972) Septic pulmonary emboli arising from a permanent transvenous cardiac pacemaker. *Chest* **61**, 503–505.

WILLIAMS G. D., BULLOCH R. T., PEARCE M. B., RATTS T. E. and KIZZIAR J. C. (1974) Long term pacing experience. In: *Current Problems in Surgery*, Part 2. Chicago, Year Book, pp. 14–17.

WILSON T. S and STUART R. D. (1965) *Staphylococcus albus* in wound infection and in septicaemia. *Can. Med. Assoc. J.* **93**, 8–16.

WITTE J., WARNKE H., DRESSLER L., VOGEL I. and OTTO H. H. (1969) Fünfjährige Erfahrungen in der Therapie des av-Blocks mit elektrischen Herschrittmachern. *Dtsch. Gesundheitsw.* **24**, 872–875.

Br. J. Surg. Vol. 62 (1975) 936–940

The efficiency of surgical masks of varying design and composition

LOUIS B. QUESNEL*

SUMMARY

Five different types of surgical mask of varying design and composition of natural and synthetic fibres were tested for their efficiency in vivo by means of a special test chamber. Contaminated particles escaping through or around the mask during speech by the wearer could be collected and sized. Analysis of the data showed that the gross efficiency of all the masks was high, but that some masks were distinctly better at small particle 'filtration' than others. There was a significant difference in efficiency between the best and worst masks. The best masks contained more fabric, were softer and were pleated, while the worst were stiffer, smaller and not pleated. Reusable cotton fabric masks were as effective as synthetic fabric masks when made to a good design.

ALTHOUGH the use of surgical masks has become routine in many clinical situations there persists a wide variety of opinions about their usefulness. Hirshfield and Laube (1941), summarizing the reports from twenty-one papers, recorded opinions ranging from a firm belief in their efficacy to denials of their usefulness in helping to prevent infection. One of the obvious reasons for the controversy is the difficulty of obtaining accurate assessments of mask efficiency, and a wide variety of techniques has been used in attempts to evaluate the effectiveness of different masks.

As early as 1935 Paine, in performing tests with masks made from natural fibres such as silk and cotton gauze, recognized the importance of particle size and found that 'high momentum droplets' could be effectively arrested by several layers of fine gauze. Mask efficiency actually increased with prolonged use. His test system involved a painted plaster cast of a face, through which were bored three holes representing the nares and partly open mouth. Into the back of the cast was fitted the wide end of a funnel, the narrow end being joined to an atomizer spray charged with a broth culture of *Micrococcus lysodeikticus*.

Shooter et al. (1959) tested one gauze (filtration) mask and two paper (deflection) masks and concluded that the three masks 'would fulfil their main purpose in protecting the patient's wound from many of the bacteria in the surgeon's mouth when the latter talked'. With deflection type masks it seemed 'probable that deflected expired air will inevitably carry some of the shed bacteria behind the head'. Their test system involved the use of 129 volunteers in a sitting position with the head isolated in a 'tent' through which a horizontal air flow was maintained. Organisms were collected on 20 Petri plates distributed in different locations on the floor of the tent chamber. From a variety of tests using exposed plate and slit sample techniques Thomas (1961) concluded that cotton gauze masks were much more efficient than paper masks in preventing the dispersal of 'small droplets and droplet nuclei'. Laundering of cotton masks increased their efficiency as filters.

Greene and Vesley (1962) designed a chamber which enabled them to test the efficiency of surgical masks under simulated *in vivo* conditions, using an Andersen (1958) cascade sampler. They found that a gauze and flannel mask was over 99·6 per cent efficient in blocking particles of diameter greater than 4 μm and 96·7 per cent efficient for particles under 4 μm.

Madsen and Madsen (1967) used a test chamber the same as that designed by Greene and Vesley (1962) to evaluate the efficiency of four different types of mask: a polypropylene-fibre mask, a polyester-rayon mask, a glass-fibre mask and a cellulose-fibre mask. Instead of the masks being worn by a human subject they were fixed to a dummy head made to average human dimensions (Churchill and Truett, 1957). To simulate sneezing or coughing a nebulizer controlled by an electronic timer was fitted inside the manikin head. A spore suspension of *Bacillus stearothermophilus* was used as the test organism. They obtained overall efficiencies of 98·8 and 98·4 per cent for the polypropylene and polyester-rayon masks respectively, with 97·3 per cent for the glass-fibre mask and 92·7 per cent for the paper mask.

There is at present a wide variety of surgical masks available in several different designs, manufactured from a variety of natural and synthetic fibres. Equally, many different claims have been made as to their likely efficiency in preventing cross-infection from wearer to patient. We decided to compare the performance of a selection of these by an *in vivo* method based on the procedure used by Greene and Vesley (1962).

Materials and methods

Sampling chamber

A chamber similar to that of Greene and Vesley's (1962) was constructed. It was made mainly from $\frac{3}{16}$-in plywood and $1\frac{1}{2}$-in angle iron (*Fig.* 1). The main box structure was 5 ft × 16-in × 16 in mounted vertically, of which the upper 4 ft was of square section, while the lower 1 ft tapered pyramidally to a 4-in square block of hardwood at the base. In the centre of the latter was fixed a piece of copper pipe of internal diameter

---

* Department of Bacteriology and Virology, University of Manchester, Manchester M14 9PT.

1 in. To this, externally, the Andersen sampler was linked by means of a piece of rubber tubing of similar internal diameter and about 5 in in length.

The top of the chamber had a square, lipped hole into which was fitted, exactly, a 10-in Vokes Super Vee Fibreglass Air Filter Panel No. E. 70802/1. The filter was seated on a foam plastic gasket to give an airtight seal. This type of filter has an efficiency of over 98·5 per cent for particles down to 6·0 μm in diameter and about 90 per cent for particles down to 1 μm.

One panel of the 'box' was divided at a point 1 ft from the top, and the 16 × 12-in panel formed was made to slide up and down in close-fitting grooves provided in the frame. The bottom of this panel and the top of the adjoining panel was cut out to form between them an eliptical hole about 6½ × 5½ in. This hole was surrounded on either half by a ¾-in thick plastic foam collar to leave a final hole of 4½ × 4 in which formed a snug fit around the neck of the subject when his head was inserted in the chamber and the sliding panel drawn down. The wall of the chamber opposite the 'head-port' was made entirely of clear Perspex to enable the subject to read a stopwatch placed on a bench outside the chamber and to prevent a feeling of claustrophobia.

The total volume of the chamber was 7·886 ft^3, of which 0·776 ft^3 was the volume enclosed by the pyramidal lower portion of the chamber. The volume from the line of entry of the head to the base of the chamber was 6·106 ft^3.

Test procedure

The procedure used was based on that used by Greene and Vesley (1962), but was not the same as we found it impossible to generate the large numbers of organisms which they claimed to be produced by uttering the words 'sing and chew' six times. Instead these trials required that the word 'chew' be repeated a total of 120 times during the space of 4 minutes. The exact procedure used was as follows:

1. Exactly 30 minutes before the time at which the masked subject was to insert his head into the test chamber, the test mask was fixed in place in the normal wearer's position. This was taken as zero time for the whole sequence.
2. At 10 minutes the chamber was flushed by running the sampler pump and drawing the air through for 5 minutes. During the whole of this period (and in fact from the day before) the head-port was covered by a cardboard plate sealed to the walls of the chamber by adhesive tape.
3. At 20 minutes the chamber was extracted for a further 5 minutes, this time with the sampler loaded with 6, 5 per cent blood-agar plates. This yielded the background count (column *a* of *Table 1*).
4. At 30 minutes less 15 seconds the head-port cover was removed, the sliding panel raised and the subject's head inserted into the chamber; the panel was closed to form a snug fit around the subject's neck.
5. At 30 minutes the sampler (loaded with 6 fresh 5 per cent blood-agar plates) was switched on, and at the same time the subject began to speak the word 'chew' at 1-second intervals for 5 seconds followed by a 5-second rest, alternating for 4 minutes (i.e. 30 enunciations per minute for 4 minutes = 120 words).
6. After the 4-minute speech sequence the subject remained mute until the total sampling time of 5 minutes had elapsed. The sampler was then switched

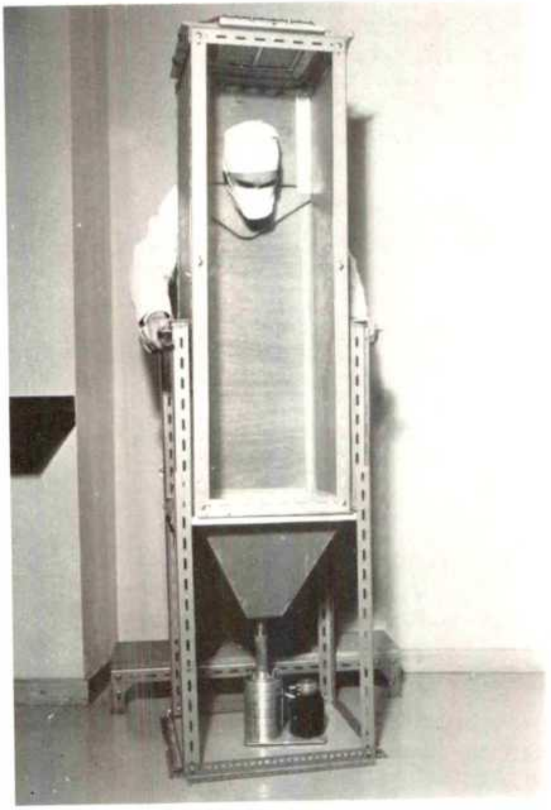


Fig. 1. The experimental chamber showing, at the top, the fibre-glass filter, the foam collar, the clear Perspex front panel and the Andersen sampler.

Table 1: COLONY COUNTS OBTAINED AT EACH SAMPLING TIME OF THE MASK TRIALS

Mask type	*a* Background	*b* Masked	*c* Post-masked	*d* Unmasked	*e* % Leak *b* of *d*	*f* % Leak *b* + *c* of *d*
Aseptex	6	91	103	2614	3·48	7·42
Cestra	22	62	101	4949	1·25	3·29
Surgine	23	109	202	8956	1·21	3·47
Filtermask	17	156	188	3747	4·16	9·18
Filtron	11	65	160	5215	1·24	4·21

Each count figure recorded represents the total colony count for four experimental trials off, the plates removed for incubation (column *b* of *Table I*) and a new set of plates loaded.

7. The subject removed his head, the head-port was sealed as before and at 40 minutes a further sample was withdrawn from the chamber, the plates removed and the sampler reloaded. These plates yielded the background count given in column *c* of *Table I.* There is no reference to such a count having been made by Greene and Vesley (1962).

8. At 48 minutes the cardboard cover was removed from the head-port and the subject reinserted his head, but this time unmasked, and procedures 5 and 6 were repeated as exactly as possible as before. This yielded the 'unmasked' counts recorded in column *d* of *Table I.*

9. At the end of the 5-minute unmasked sampling period the headport was again sealed.

Only one such mask trial was made on each day and blood-agar plates were poured freshly each day. They consisted of a bottom layer of Oxoid blood-agar base and a top layer of the same agar but containing 5 per cent defibrinated horse blood. The total volume in each plate was exactly 27 ml as required in the instructions for use of the Andersen sampler. Incubation was carried out at 37 °C for 24 hours.

Surgical masks

The masks tested were:

1. Aseptex mask No. 1800 (3M Company, Medical Products Division). This is a 'rigid' cup-shaped mask of bonded polyester and rayon fibres held in place by an elastic band.
2. Cestra mask (Robinsons of Chesterfield) made from four-ply cotton muslin. The entire batch of these masks was subjected once to the normal hospital laundry routine for articles of this type at the Manchester Royal Infirmary. They were steam pressed and packed in 'sterilization pack' paper bags, but were not autoclaved.
3. Surgine (Johnson & Johnson Ltd). Mask of three-ply construction, outer layers bonded rayon, inner glass fibre; three pleats.
4. Filtermask E-Z breathe (Deseret Pharmaceutical Co. Inc.). Mask of three-ply construction, outer layers cellulose, inner glass fibre; simple folded design.
5. Filtron (3M Company, Medical Products Division). Mask of three-ply construction, outer layers cellulose, inner of polypropylene fibre; single box-pleat design.

Except for the Cestra mask they are all of the single-use, disposable variety, and are used directly from the boxes in which they are purchased. Except for the Aseptex they are held in place by pairs of fabric ties. All the disposable masks also have metal contour strips, which are pressed well down across the nose and cheeks in use.

Four trial runs were performed with each mask type, and all the masks were worn by the same subject throughout the investigation.

Counting

The colony counts recorded for each plate in each trial were obtained by using the 'positive hole count' method described in the instructions supplied with t Andersen sampler and a statistical correction appli according to the tables given by Peto and Pow (1970).

Results

The test procedure described yielded four sets colony counts for each trial. The Andersen sampl separates contaminant particles into six different si ranges which comprised each set as follows: plate >9·2 μm; plate 2, 5·5–9·2 μm; plate 3, 3·3–5·5 μ plate 4, 2·0–3·3 μm; plate 5, 1–2 μm; plate 6, <1 μ

In *Table I* the counts recorded are the totals for size ranges obtained in a total of 4 trials in each cas The 'background' count represents the number organisms entering the chamber while the head-p was open plus any organisms which passed throu the filter in the roof of the chamber. The 'maske count gives the total colonies obtained during t sampling periods when the masks were worn, wh the 'post-masked' count represents the residual a borne population still present in the chamber betwe 6 and 11 minutes after the end of the speech sequen giving rise to the organisms. The 'unmasked' cou represents the output of organisms resulting from t speech sequence and able to be collected within 5-minute sampling period similar to that used for t 'masked' count.

Table I shows that if the leakage of organis through or around the mask is calculated from t 'masked' and 'unmasked' data, there is no differen in efficiency between the Cestra, Surgine and Filtr masks, while the Aseptex and Filtermask desig appear to be somewhat less efficient. The same gene conclusion may be drawn if the calculations are bas on the total leakage, i.e. the 'masked' and 'po masked' counts as a percentage of the 'unmaske counts.

From *Table II* some comparison of efficiencies m be made in regard to performance in filtering lar particles (>3·3 μm) and smaller particles. It can seen that all the masks show a high degree of efficien of about 99 per cent in large particle filtration, b considerable differences in small particle filtrati efficiency exists. Again, the Aseptex and Filterma designs performed worst, however the data we calculated.

In *Table III* overall efficiencies are listed taking particles together, Aseptex and Filtermask aga performing the least well. Statistical tests of significan (*t*-test) performed on the data for total leakage valu showed no significant difference in efficiency betwe Cestra, Surgine and Filtron, while the difference w significant at the $P = 0{\cdot}05$ level between Filtron ar Filtermask, and at $P = 0{\cdot}1$ between Filtron ar Aseptex but just outside the significance level $P = 0{\cdot}05$.

Fig. 2 shows the distribution of particle sizes four from bacteria-containing droplets expelled from t subjects' mouth and nares during the course of t trials reported in this paper. It shows a marked different distribution from that obtained by t aerosolization of bacteria (or spores) using mechanical devices of various kinds, which has been drawn from the results of Garrow et al. (1971) using *Serratia marcescens*. It is not surprising that they differ significantly and that the distribution for the naturally expelled population should be skewed markedly to the left (i.e. towards large particle size) since the bacteria of the normal respiratory tract flora typically grow in clusters or aggregates, e.g. the Corynebacteria, streptococci, staphylococci, Neisseria, etc.

The histogram of our data was calculated from a total of 25 481 particles (corrected count) which were expelled during 2400 utterances of the word 'chew', giving an average of 10–11 colony-forming units per word.

Discussion

In deciding which test procedure should be used for the investigation of mask efficiency it was necessary to consider carefully what were the main objectives. We did not think a test of filtration efficiency of merely the mask material under *in vitro* conditions such as those devised by Rubbo and Abbott (1968) would be adequate since in use the mask is 'fixed' around an irregular surface (the face) and a certain amount of leakage around the edges would occur. Also, to pass a standard aerosol through clamped samples of fabric at a steady flow rate did not seem to be a good approximation of the situation *in vivo*.

Also, it was thought necessary that the mask should be subjected to the effects of abrasion and moisture which would obtain during use by a human subject, so on this basis all the manikin methods described in the literature were ruled out. Again, because of the problems of uneven distribution of expelled organisms, some of which passed through the mask and some of which were expelled 'backwards' around the edges, all methods involving freely exposed agar plates were also ruled out.

Therefore, in order, to obtain *in vivo* conditions a human subject was considered essential, and in order to collect all the organisms which leaked either through or around the mask an enclosed air volume which could be 'swept' over the receiving plates was also considered necessary. The special test chamber and Andersen sampler met these requirements.

We modified the procedure of Greene and Vesley (1962), who first used this type of chamber, in a number of ways. First, it was thought essential that the mask be worn for at least a reasonable period of time before commencing the tests as some fibres are hygroscopic and would perform differently when 'saturated' with moisture from, for example, exhaled air. A time of 30 minutes was chosen so that the masks would be already moistened and contaminated with organisms before the tests began.

Secondly, we found that saying the phrase 'sing and chew' six times (Greene and Vesley, 1962) produced very few organisms and so we changed the speech sequence to 120 repetitions of the word 'chew'. Also, since this sequence lasted for 4 minutes of the 5-minute sampling period, and the total 5-minute sample was only 5 ft^3 out of a chamber volume of nearly 8 ft^3, a subsequent 5-minute sampling period, the 'post-masked' sample, was added to the procedure.

Table I, which lists the counts obtained for the various masks, shows a number of interesting features. First, the background counts show that not more than an average of 6 contaminant particles per 5-minute sampling period were likely to enter the chamber adventitiously, i.e. through the filter or head-port. Strictly speaking, these adventitious contaminants

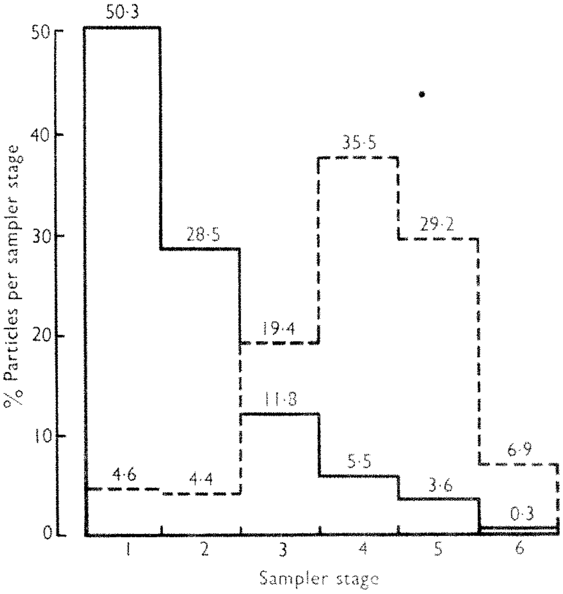


Fig. 2. The distribution of 'colony-forming units' by particle size. The histogram with entire margin was obtained by collecting together all the 'unmasked' counts and arranging the data as percentage of the total count for each stage of the Andersen sampler. The total count was 25 481. The histogram with broken margin gives the distribution of colony-forming units by particle size for aerosolized *Serratia marcescens* as found by Garrow et al. (1971).

Table II: LEAKAGES CALCULATED IN THE PARTICLE SIZE RANGES GIVEN FOR EACH MASK TYPE

	% Leak *b* of *d**		% Leak *b* + *c* of *d**	
Mask type	>3·3 µm	0–3·3 µm	>3·3 µm	0–3·3 µm
Aseptex	1·13	20	2·1	44·9
Cestra	0·62	10·96	1·37	32·89
Surgine	0·28	10·39	0·54	32·28
Filtermask	0·70	27·82	1·65	60·66
Filtron	0·23	11·73	0·63	42·39

* *See Table I.*

Table III: CALCULATED FILTRATION EFFICIENCY OF THE VARIOUS MASKS; ALL SIZES OF PARTICLES

Mask type	% Efficiency based on *b* and *d* data only*	% Efficiency based on *b* + *c* and *d* data*
Aseptex	96·5	92·6
Cestra	98·8	96·7
Surgine	98·8	96·5
Filtermask	95·8	90·8
Filtron	98·8	95·7

* *See Table I.*

would also be present during the other count periods to give an artificially raised count of leakage organisms. It would be possible to make a notional correction for this, but it was thought better to omit this and state that the efficiencies recorded were therefore slightly less than the true efficiencies of the masks concerned. On this basis it was interesting to note that the percentage leak obtained is nevertheless very low in absolute terms (column *e*, *Table I*), and if only large particles are considered, extremely low (*Table II*).

Secondly, in every case the 'post-masked' count was higher than the 'masked' count. This demonstrated two points, viz. that the initial sampling period was inadequate and that viable organisms could remain in aerosolized suspension for a considerable time. Greene and Vesley (1962) did not include a 'post-masked' count in their trials so it is not known how many of these organisms were missed by them. Separate tests showed that in our experiments the number of organisms still remaining after this second 'post-masked' sample was of the same order as the background count.

When the 'filtration' efficiency of the masks is examined relative to the different size ranges of large (> 3·3 μm diameter) and small (< 3·3 μm) particles it can be seen from *Table II* that large particle filtration is extremely efficient in all cases, while small particle filtration is comparatively inefficient, and that even the best masks were only 89–90 per cent efficient. Analysis of the data also reveals that the 'post-masked' counts in the case of Filtron and Surgine masks are about 2·5 and 2 times as great as the 'masked' counts, but only 1·5 times as great for the Cestra mask. This may be an indication that very fine filters generate small particles, which may be caused either by splitting of large particles as they impact upon the mesh or by filling the pores with liquid which then bubbles out and bursts under further pressure—the 'bubble tube' effect. It may well be that the Cestra mask was superior in performance because it was absorbant and did not readily permit the build-up of liquid films which would contribute to the 'bubble-tube' effect.

Table II also shows that the Aseptex and Filtermask designs had about half the small particle efficiency as the other 3 masks. We think that it is relevant in this regard that both of these masks were much narrower than the others, covering far less an area of the cheeks. In addition, they were both unpleated and rather stiff. These two factors would contribute to an increased leakage of organisms around the edges of the mask in that small particles would be more readily deflected backwards and more easily escape. Put conversely, it would appear that pleating contributed significantly to the efficiency of the mask in the case of the Filtron and Surgine, and the Cestra mask, while not pleated, was soft and extended well back over the cheeks and under the chin, covering a larger area than any of the other masks.

It should also be remembered that particles less than 3 μm in diameter will not easily fall on their own account, for example, into a wound during surgery. On the other hand, particles larger than 5 μm are very unlikely to enter the lungs, so that small particle inhalation would be the main hazard in situations of poor ventilation where open wounds were not involved.

A broad summary of the overall data is given in *Table III* and we may make the following general conclusions from the investigation:

1. The overall efficiency of all the masks is high, approaching 99 per cent for the best designs, viz. Cestra, Filtron and Surgine.
2. Large particle filtration efficiency was similarly high in all cases.
3. Small particle filtration efficiency was considerably lower, being worst in the Aseptex and Filtermask designs.
4. Inefficiency was probably affected as much by stiffness, lack of pleating and size as by deficiencies in 'filtration'.
5. Cotton fabrics may be as effective as synthetic fabrics when incorporated in a good mask design.

Acknowledgement

My sincere thanks are due to Mr Dennis Coupes for his expert technical assistance.

References

ANDERSEN A. A. (1958) New sampler for the collection, sizing and enumeration of viable airborne particles. *J. Bacteriol.* **76**, 471–484.

CHURCHILL E. and TRUETT B. (1957) WADC Technical Report. No. 56-261. Astia Document No. 110629.

GARROW C., STEPHENS L. J. and EWING M. R. (1971) Evaluation of surgical masks: the potential of resin treated wool. *Surgery* **69**, 881–883.

GREENE W. and VESLEY D. (1962) Method for evaluating effectiveness of surgical masks. *J. Bacteriol.* **83**, 663–667.

HIRSHFIELD J. W. and LAUBE P. J. (1941) Surgical masks, an experimental study. *Surgery* **9**, 720–730.

MADSEN P. O. and MADSEN R. E. (1967) A study of disposable surgical masks. *Am. J. Surg.* **114**, 431–435.

PAINE C. J. (1935) The aetiology of puerperal infection with special reference to droplet infection. *Br. Med. J.* **1**, 243–246.

PETO S. and POWELL E. O. (1970) The assessment of aerosol concentration by means of the Andersen sampler. *J. Appl. Bacteriol.* **33**, 582–598.

RUBBO S. D. and ABBOTT L. R. (1968) Filtration efficiency of surgical masks: a new method of evaluation. *Aust. NZ J. Surg.* **38**, 80–83.

SHOOTER R. A., SMITH M. A. and HUNTER J. W. (1959) A study of surgical masks. *Br. J. Surg.* **47**, 246–249.

THOMAS C. G. A. (1961) Efficiency of surgical masks in use in hospital wards. *Guys Hosp. Rep.* **110**, 157–167.

Br. J. Surg. Vol. 62 (1975) 941–944

Identification of talc on surgeons' gloves and in tissue from starch granulomas

W. J. HENDERSON, C. MELVILLE-JONES, W. T. BARR AND K. GRIFFITHS*

SUMMARY

Particles of talc have been identified on the route surface of surgeons' rubber gloves and in sections of tissue classified as 'starch' or 'foreign body' granulomas. This analytical study indicates that under certain circumstances these granulomas could have been caused by talc contamination.

THE recognition that the use of talc as a surgical glove powder was responsible for the postoperative development of peritoneal adhesions and tissue granulomas at the site of operation (Lichtman et al., 1946; Eismann et al., 1947) stimulated the search for an inert absorbable substitute, and resulted in its eventual replacement by a starch powder (Lee and Lehman, 1947; Postlethwaite et al., 1949) which initially appeared to produce no ill-effects within the peritoneal cavity. There have, however, been numerous reports over the past two decades suggesting that the use of starch powder could also result in a granulomatous reaction similar to that produced by talc (Snierson and Woo, 1955; McAdams, 1956; Nash, 1971; Neely and Davies, 1971; Cohen and Safaie-Shirazi, 1973). Starch granuloma peritonitis secondary to the glove powder reaction has now become recognized as a clinical entity (Sobel et al., 1971), and Taft et al. (1970) suggested that the severity of the condition may be related to the type of starch used. The starch powder has also been shown to produce granulomas and adhesions in experimental animals (Lee et al., 1952; Perper et al., 1971; Ignatius and Hartmann, 1972).

However, the results reported here indicate that starch particles may not always be responsible for the development of the granuloma peritonitis and that contaminants of the dusting powder used on the surgeons' gloves must be taken into consideration.

Materials and methods

A modified extraction replication technique (Henderson, 1969; Henderson and Griffiths, 1972) was used to prepare a particulate preparation from histological sections of tissue reported to be 'starch', 'foreign body' or 'suspected talc' granulomas. After removal of the wax with xylene and dehydration with alcohol, the tissue section was ashed on a microscope slide in an oven by slowly increasing the temperature to 500 °C and allowing oxygen to flow over the section. After incineration, the particles were removed using a film of 7 per cent polyvinyl alcohol (PVA). A carbon film was deposited on to the PVA film *in vacuo*. The PVA was then dissolved in a hot water-bath, leaving the particulate material trapped in the carbon film. Areas of interest were then localized on reference electron microscope grids and a second carbon coat deposited to stabilize the particles under the condensed electron beam required for micro-analysis. Particles were analysed in the electron microscope micro-analyser (EMMA-4; AEI) as previously described (Henderson et al., 1975).

A similar extraction technique was used to obtain a particulate preparation from the surface of a series of surgeons' gloves manufactured by different companies. PVA was allowed to flow over specific areas of the gloves and then allowed to harden. The resulting film containing the particulate matter was removed and examined as described above.

Table I: PARTICLE RECOVERY FROM STARCH GRANULOMAS

Stomach	E-3	V-6	U-6	U-4	I-6
	26	4	5	2	3
Gallbladder	M-1	J-2	B-4	U-6	K-1
	18	4	0	1	0
Omentum	L-3	I-1	X-5	2-5	X-1
	24	12	0	0	1
Appendix	P-1	I-1	U-1	U-6	T-6
	3	4	8	3	0
Peritoneal tissue	Q-2	Q-4	8-5	6-2	Y-2
	3	16	56	18	7
Peritoneum nodules	V-4	O-4	3-6	9-1	I-6
	6	1	3	1	0

The upper figure denotes the individual reference grid square examined, and the lower figure the number of talc particles/grid square.

Results

Light microscopy of sections from 6 starch granulomas studied showed the classic rounded particles with Maltese cross birefringence. The sections were also shown to contain significant quantities of talc particles. Talc, a magnesium silicate, was identified in the electron microscope micro-analyser by the characteristic Si : Mg ratio of approximately 3 : 1 (Henderson et al., 1973). *Table I* shows the quantitative amount of talc particles located on numbered reference electron microscope grid squares in the series of sections studied. Localization of high concentrations in a particular area of a grid could often be related to the presence of giant cells recognized by routine optical microscopy of adjacent histological sections. A typical area of particles within a grid square is shown in

---

* W. J. Henderson, C. Melville-Jones and K. Griffiths: Tenovus Institute for Cancer Research, Welsh National School of Medicine, Cardiff.
W. T. Barr: Department of Pathology, University Hospital of Wales, Cardiff.

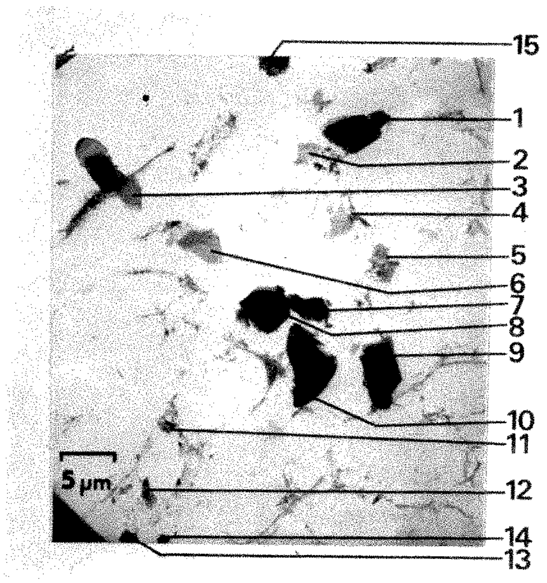


Fig. 1. Particles recovered from peritoneal tissue of a case of starch granuloma. The analytical composition of the particles is shown in *Table II*.

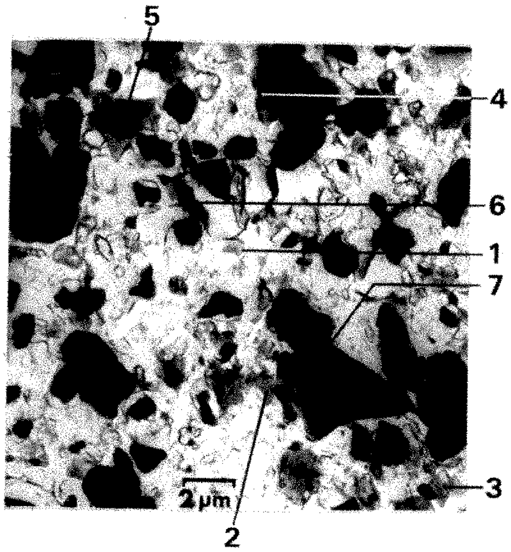


Fig. 2. Particulate material extracted from the external surface of a surgeon's glove. The individual analysis of the particles is shown in *Table V*.

Fig. 1. Analytical data for this series of particles are given in *Table II*. Tissue sections classified after histological examination as 'foreign body' granulomas rather than specifically implicating talc or starch were also studied. The number of particles of talc identified in these sections are shown in *Table III*. An average of two particles/grid square gives approximately 1600 particles/mm² tissue section. Three tissue sections classified as suspected talc granulomas (*Table IV*) were shown to contain large numbers of talc particles/grid square.

Surgeons' gloves (20 pairs) from companies in the United Kingdom were studied using the techniques described. These gloves were manufactured between 1973 and late 1974. At the same time 4 sample pairs of gloves from a company in Austria and another in the United States were obtained for simple comparative studies. *Fig.* 2 shows a typical group of particles extracted from the surface of a glove from a British manufacturer. The analysis of these particles is given in *Table V*. This was a typical result showing contamination of 8000 talc particles/mm² of glove

Table II: ELEMENTAL COMPOSITION OF THE PARTICLES SHOWN IN FIG. 1

	Particle (X-ray counts/100 sec)						
Particle	Mg	Si	Al	S	Ca	Fe	Si/Mg
1	404	1369		34	16	64	3·388
2	42	93	30	27		10	
3	205	682				29	3·327
4	87	311				15	3·575
5	93	295	97	24		39	
6	151	493		14		16	3·265
7	1090	4049				52	3·715
8	849	2863				42	3·372
9	1117	3703				42	3·315
10	1855	6232				143	3·3595
11	213	748			72	53	3·5117
12	300	862		22	14	29	2·873
13	356	1226		26	41	52	3·444
14	1175		636		152	100	
15	703	2310				41	3·286

Table III: PARTICLE RECOVERY FROM FOREIGN BODY GRANULOMAS

Sebaceous cyst	2-6	O-3	V-5	G-5	G-1
	1	1	2	5	8
Lymph node	Q-6	Q-5	R-5	R-1	Q-2
	2	1	4	0	0
Ovary	X-5	X-6	4-1	8-2	Y-3
	7	1	73	20	18
Thigh (cyst)	R-1	M-6	V-3	D-4	K-3
	2	2	0	0	1
Ovary	W-5	X-6	V-6	J-3	2-6
	1	3	2	0	0

The upper figure denotes the individual reference grid square examined, and the lower figure the number of talc particles/grid square.

Table IV: PARTICLE RECOVERY FROM SUSPECTED TALC GRANULOMAS

Cervix	7-2	P-4	V-5	J-5	T-4
	40	121	90	110	3
Small intestine	R-5	R-3	Q-2	H-2	P-2
	108	20	52	16	2
Stomach	3-5	3-6	9-6	5-2	4-3
	7	4	5	4	1

Table V: ELEMENTAL COMPOSITION OF PARTICLES SHOWN IN FIG. 2

Particle no.	Particle (X-ray counts/100 sec)		
	Mg	Si	Si/Mg
1	128	399	3·117
2	452	1414	3·127
3	1690	4980	2·947
4	809	2475	3·059
5	856	2629	3·039
6	1868	5413	2·889
7	2182	6676	3·060

face. However, results varied with different ches of gloves. It was interesting that in the nples of gloves manufactured in other countries, no tamination was found on the Austrian gloves, ereas the samples from the American manufacturer e found to be heavily contaminated and a second A extraction was often necessary to allow singleticle analysis. It must be remembered that only a / limited number of gloves have been studied.

)ther elements detected in large amounts on the /e surface were zinc and sulphur. Whole fossilized coliths were often observed on the surface, and ıld appear to be responsible for the calciumtaining granules that were generally detected on ish gloves.

cussion

se results clearly indicate that the surgeons' gloves lied, manufactured in Britain and the United es, were contaminated by particles of talc. These ticles present on the outer surface of the gloves e extremely small, some 20 nm in diameter, and it ıld seem that in the manufacturing process the r systems used were inadequate to prevent access hese fine talc crystals. The normal procedures used checking such contamination may again be lequate to identify these particles and obviously not possess the resolving or analytical capacity of electron microscope micro-analyser. The gloves nufactured in the United States had even more talc ticles per unit surface area, whereas the Austrian /es studied appeared to be uncontaminated. The nt of such contamination cannot really be ssed from a preliminary study of this nature, but results of these investigations do suggest that it uld not be assumed that foreign body granulomas /hich starch can be identified are necessarily due to ch. Submicroscopic particles of talc which have n identified may also be concerned.

urthermore, analysis of the particulate content of a es of histological sections of tissue classified as ch or foreign body granulomas also showed that e tissues contained talc particles. This extraction nique has been used for the study of asbestos fibres nesotheliomas (Henderson et al., 1969), talc in rian tissue (Henderson et al., 1971; Griffiths et al., 3) and the particulate matter in tissue from nach tumours removed from Japanese men nderson et al., 1975). The use of EMMA-4 vides the sophisticated analytical technique by ch individual particles can be identified. Whether granulomatous lesions, the cause of which has n attributed to the presence of starch, resulted ead from the presence of contaminating talc on the geons' gloves cannot at present be decided. There several laboratory and clinical studies which icate that starch particles *per se* can produce nulomas and adhesions within the peritoneal ity. The findings reported here merely draw ntion to the fact that talc contamination of the ves must be seriously considered in relation to this drome.

It is interesting that earlier studies (Henderson et al., 1971; Griffiths et al., 1973) revealed the presence of talc particles deeply embedded in tissues of the female genital tract, and in particular in the ovary and in ovarian tumours. Although contamination of the surgeons' gloves initially made this work suspect, further recent analyses undertaken with even greater thoroughness and care confirmed the presence of talc particles embedded deep within ovarian tissue. It has been suggested that the source of this talc could well be various types of contraceptives and that the route of entry is the fallopian tube. In relation to this, a case has been reported of a young woman with acute peritonitis whose peritoneum was covered in granulomatous lesions which were found to contain corn starch (Saxen et al., 1963). The source of the starch was found to be the lubricant of her husband's contraceptives.

It is important to know that the principal British producer of surgeons' gloves, on being advised of these findings, located the source of the talc contamination. It was in a process unrelated to and physically separated from the process for the manufacture of the gloves. The use of talc has now been eliminated, but the company hopes to introduce a system whereby possible glove contamination can be routinely monitored.

Acknowledgements

The authors are grateful to the Tenovus Organisation for generous financial support and to Professor E. D. Williams, Department of Pathology, Welsh National School of Medicine, Cardiff, for his cooperation and interest in this study.

Mr J. W. Miller, Department of Pathology, St Bartholomew's Hospital, London, kindly provided some of the tissue sections.

References

COHEN W. N. and SAFAIE-SHIRAZI S. (1973) Starch granulomatous peritonitis. *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **117**, 334–339.

EISMANN B., SEELIG M. G. and WOMACK N. A. (1947) Talcum granuloma; frequent and serious complication. *Ann. Surg.* **126**, 820–832.

GRIFFITHS K., HENDERSON W. J., CHANDLER J. A. and JOSLIN C. A. F. (1973) Ovarian cancer: some new analytical approaches. *Postgrad. Med. J.* **49**, 69–72.

HENDERSON W. J. (1969) A simple replication technique for the study of biological tissues by electron microscopy. *J. Microsc. (Oxf.)* **89**, 369–372.

HENDERSON W. J., CHANDLER J. A., BLUNDELL G., GRIFFITHS C. and DAVIES J. (1973) The application of analytical electron microscopy to the study of diseased biological tissue. *J. Microsc. (Oxf.)* **99**, 183–192.

HENDERSON W. J., EVANS D. M. D., DAVIES J. D. and GRIFFITHS K. (1975) Analysis of particles in stomach tumours from Japanese males. *Environ. Res.* **9**, 240–249.

HENDERSON W. J. and GRIFFITHS K. (1972) Shadow casting and replication. In: HAYAT M. A. (ed.) *Principles and Techniques of Electron Microscopy, Biological Applications*, Vol. 2. New York, Van Nostrand Reinhold, pp. 151–193.

HENDERSON W. J., HARSE J. and GRIFFITHS K. (1969) A replication technique for the identification of asbestos fibres in mesotheliomas. *Eur. J. Cancer* **5**, 621–624.

HENDERSON W. J., JOSLIN C. A. F., TURNBULL A. C. and GRIFFITHS K. (1971) Talc and carcinoma of the ovary and cervix. *J. Obstet. Gynaecol. Br. Commonw.* **78**, 266–272.

IGNATIUS J. A. and HARTMANN W. M. (1972) The glove starch peritonitis syndrome. *Ann. Surg.* **175**, 388–397.

LEE C. M. jun., COLLINS W. T. and LARGEN T. L. (1952) Reappraisal of absorbable glove powder. *Surg. Gynecol. Obstet.* **95**, 725–737.

LEE C. M. jun. and LEHMAN E. P. (1947) Experiment with non-irritating glove powder. *Surg. Gynecol. Obstet.* **84**, 689–695.

LICHTMAN A. L., MCDONALD J. R., DIXON C. F. and MANN F. C. (1946) Talc granuloma. *Surg. Gynecol. Obstet.* **83**, 531–546.

MCADAMS G. B. (1956) Granuloma caused by absorbable starch glove powder. *Surgery* **39**, 329–336.

NASH D. F. E. (1971) Glove powder. *Br. Med. J.* **3**, 183.

NEELEY J. and DAVIES J. D. (1971) Starch granulomatosis of peritoneum. *Br. Med. J.* **3**, 625–629.

PERPER J. A., PIDLAON A. and FISHER R. S. (1971) Granulomatous peritonitis induced by rice starch. *Am. J. Surg.* **122**, 812–817.

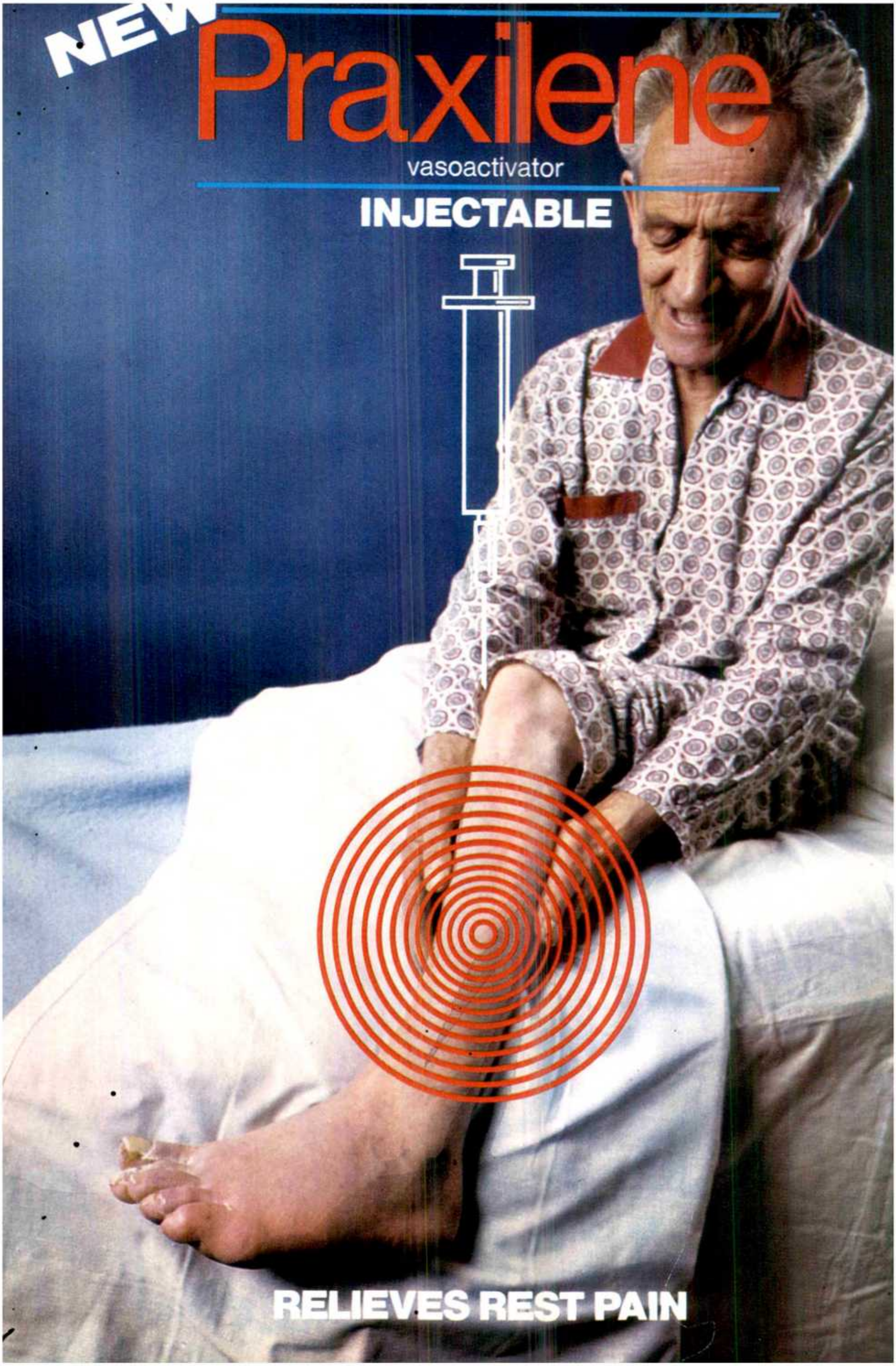
POSTLETHWAITE R. W., MCRAE J. T., WILLIAMS R. W., DEATON W. R. and CORNATZER W. E. (1949) Absorbable starch glove powder. *Am. J. Surg.* **78**, 510–513.

SAXEN L., KASSINEN A. and SAXEN E. (1963) Peritoneal foreign body reaction caused by condom emulsion. *Lancet* **1**, 1295–1296.

SNIERSON H. and WOO Z. P. (1955) Starch powder granuloma: report of two cases. *Ann. Surg.* **142**, 1045–1050.

SOBEL H. J., SCHIFFMAN R. J., CAMDEN N. J., SCHWARZ R. and ALBERT W. S. (1971) Granulomas and peritonitis due to starch glove powder. *Arch. Pathol.* **91**, 559–568.

TAFT D. A., LASERSOHN J. T. and HILL L. D. (1970) Glove starch granulomatous peritonitis. *Am. J. Surg.* **120**, 231–236.


NEW
Praxilene
vasoactivator
INJECTABLE
RELIEVES REST PAIN

NEW

for peripheral vascular disorders

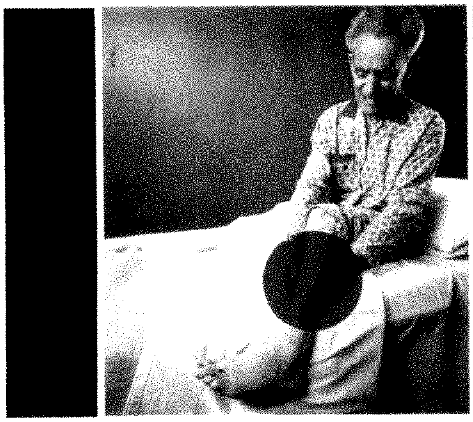
Praxilene

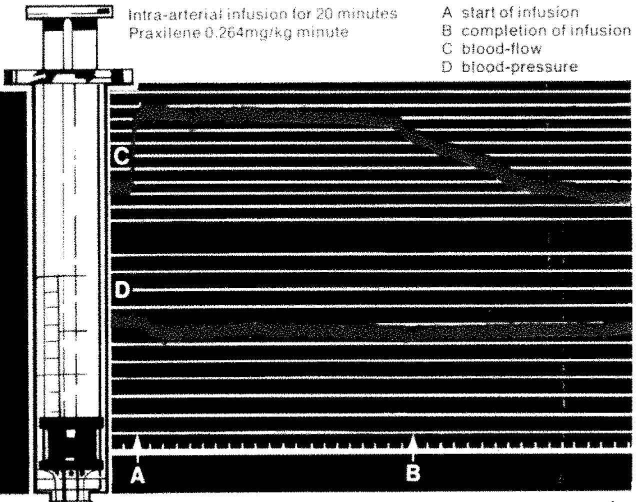
vasoactivator

INJECTABLE

RELIEVES REST PAIN

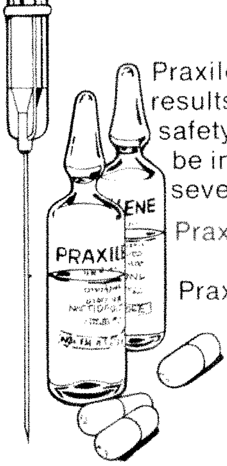
by flushing out pain producing metabolites
by improving blood-flow – without affecting blood-pressure
by a unique metabolic activity





Fast relief
Praxilene administered parenterally (Intra-arterial; Intravenous; Intramuscular) can give relief of pain within as short a time as one week, in many cases.

Prolonged relief
Relief of pain is prolonged: at the same time the collateral circulation is given the opportunity to develop, resulting in an improved blood supply to the affected limb.



Praxilene has produced excellent results because it has a very wide safety margin and the dosage can be individually tailored to the severity of the disorder.

Praxilene: Unique Vasoactivator

Praxilene: Naftidrofuryl: available as 40mg ampoules and 100mg capsules.

Full prescribing information and dosage schedule on request

Lipha (UK)
West Drayton, Middlesex
Telephone: West Drayton 49331/2

Br. J. Surg. Vol. 62 (1975) 945–949

The effect of metal clips on the tensile properties of healing skin wounds

I. D. HARRISON, D. F. WILLIAMS AND A. CUSCHIERI*

SUMMARY

The effects of nylon sutures and metal skin clips on the tensile properties of healing skin wounds have been studied in the pig. Wounds closed with clips have significantly poorer mechanical properties at 5, 7 and 14 days after wounding than similar wounds in the same animal closed with interrupted nylon sutures. This difference increased progressively with the period of retention of the clips. It is also shown that in equivalent groups of 14-day wounds, those in which clips were retained after the seventh day had a lower tensile strength, poorer ability to absorb energy and a lower elastic modulus than similar wounds where clips had been removed early. No such adverse effect was noted with nylon sutures.

METAL clips have been used for the closure of skin wounds for many years. The majority of surgeons have tended to restrict their use to wounds in the head and neck and have removed them at the earliest possible time. Early removal would appear to have been based on one of two possibilities, both untested: either that clips, being non-penetrating, allow healing to progress more rapidly than conventional sutures, or that clips, being potentially damaging, should be restricted to rapidly healing areas where early removal is possible. The increasing usage of clips and the appearance in the literature of reports of their use for general abdominal incisions (Annis, 1973) suggested that a critical assessment of their effects upon healing skin wounds should be made. We believe that the mechanical properties are the most important features to be considered in a healing wound.

The mechanical properties of wounds have been extensively investigated over many years. Only relatively recently, as a result of the work of Beckwith et al. (1963) and Glaser et al. (1965) in the United States and Gibson et al. (1965) in the United Kingdom, have the precise physical and engineering principles involved in testing the tensile properties of biological tissues been clarified.

There are three stages in the experimental procedure that require considerable care if meaningful results are to be obtained. First, since the mechanical properties of skin change very rapidly with time after removal from the body each specimen should be tested at the same time after removal. It is clearly impossible to cut, measure and test a large number of specimens simultaneously. However, since these changes are temperature dependent, rapid freezing of the specimens in liquid nitrogen at −196 °C, which halts this deterioration (Marangoni et al., 1966), allows individual specimens to be thawed separately when required for testing. Thus, a standard warm deterioration time may be used for all specimens.

Secondly, it is important to define the parameters which have to be measured and to choose the optimum conditions for their measurement. The mechanical characteristics of wounds (or normal skin) may be described in terms of four parameters:

1. *Maximum tensile strength*: This is the load per unit cross-sectional area of scar required to rupture the specimen (units: g/mm^2).
2. *Maximum tensile strain*: The degree by which the specimen elongates prior to rupture as a proportion of its initial length (units: mm/mm).
3. *Energy absorption*: The total amount of work which must be done on the specimen by the applied force, per unit volume, to cause rupture (units: $g\ mm\ mm^{-3}$).
4. *Modulus of elasticity*: This indicates the ratio of stress to strain when the specimen undergoes elastic deformation. The higher the modulus the 'stiffer' or less elastic is the specimen (units: g/mm^2).

All these parameters should be measured to characterize each specimen fully. As shown by their definitions, they are expressed in terms of the dimensions of the specimen tested, being either area, volume or length dependent. Much of the pioneering work (Sandblom, 1944; Douglas, 1952) measured only the breaking strength of wounds, the cross-sectional area of the scar not being measured. It is now realized that unless the dimensions are known, it is impossible to be sure that differences noted in breaking strength are real rather than apparent, since a greater thickness of some specimens can produce a greater breaking strength without any change in the true tensile properties. The measurement of the dimensions of the specimen is not straightforward since the application of any mechanical measuring device (e.g. micrometer) will distort the specimen, giving fallacious results. Indirect techniques such as photography are therefore necessary.

Finally, skin is a mechanically complex material exhibiting visco-elastic properties that vary with the strain rate. Forrester (1973) has discussed the methods available for controlling strain rate. Because of the complex nature of the material under test and the fact that the wound itself is heterogeneous it is vital that sufficient observations are made of each wound for a thorough statistical analysis to be carried out.

---

* Departments of Surgery and Dental Sciences, University of Liverpool.

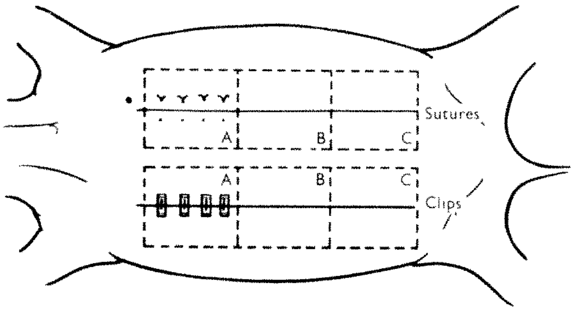


Fig. 1. Ventral surface of pig showing position of the two wounds and the areas (*A*, *B* and *C*) excised for tensile testing at different time periods.

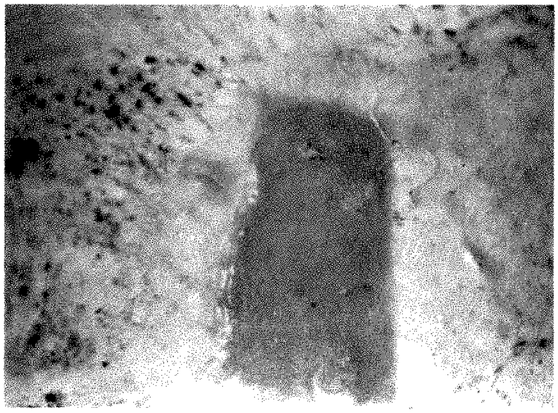


Fig. 2. Clean and granulated defect 1 week after excision of the wound area.

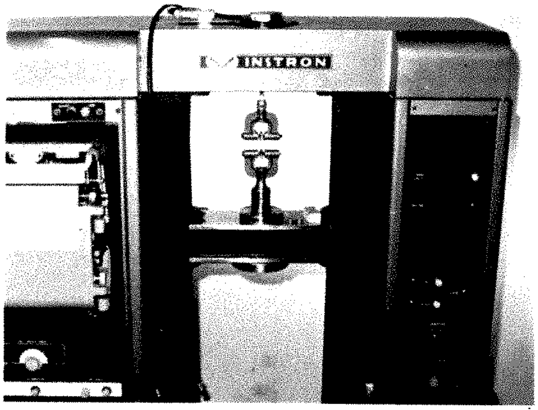


Fig. 3. Instron tensile testing apparatus showing specimen grips.

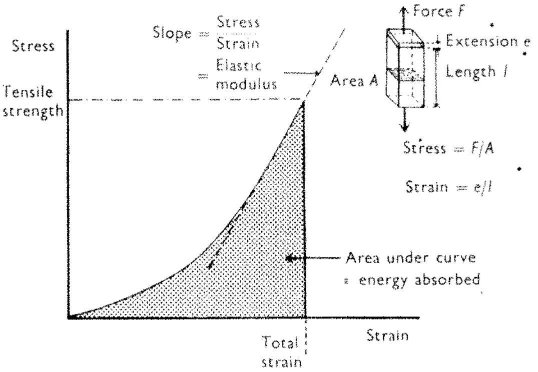


Fig. 4. Idealized stress/strain curve obtained with skin wound specimen, indicating the method of calculation of the properties described in the text.

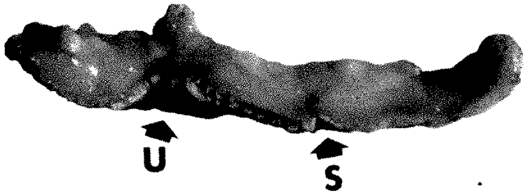


Fig. 5. Specimen excised from 7-day clip-closed wound cut ready for tensile testing showing ulceration (*U*) at site of clip teeth. *S*, Position of scar.

Materials and methods

Ten female Large White/Landrace cross-bred piglets, weighing 18–25 kg, were used in the trial. The pig was chosen for its relatively large size, lack of attachment of the skin to the panniculus carnosus and the close morphological similarity between its skin and that of man (Hartwell, 1955).

Two standardized linear incisions were created equidistant from the midline on the ventral surface of each animal. The incisions passed into the subdermal fat but did not divide the panniculus carnosus. In 8 pigs the wounds were 180 mm in length, and in each of these animals one wound was closed with 18-mm stainless steel Clay-Adams skin clips (Avlox, ICI) and the other with interrupted monofilament nylon mattress sutures (2/0 Ethicon), both being at 1·5-cm intervals. The nylon sutures entered the skin 1 cm from the wound margin and passed into the subdermal fat. The clips were applied from their specially designed applicator, thus avoiding variations in pressure of the clips on the skin. Wounding was carried out under general anaesthesia using strict aseptic technique, and during the healing period wounds were dressed with Elastoplast Airstrip dressings. A normal diet was taken throughout the trial.

For study each wound was divided into three equal areas, each containing four clips or four sutures (*Fig.* 1). One area of each wound was excised for mechanical testing after 1 week and another after 2 weeks' healing. The final area was also tested after 2 weeks' healing but differed in having had the clips or sutures removed on the seventh day, healing continuing in their absence for the final week. Any differences in the two groups of 2-week wounds should indicate whether the presence of clips or sutures aids or hinders the gain of tensile properties of wounds. The relative positions of the various wound areas were randomized.

The defect created by excision of an area of the wound was left unclosed but covered with a sterile non-stick dressing (Melalin) and isolated from the remainder of the healing wound by a waterproof dressing. It was felt that to attempt to close the defect would so distort adjacent tissues that the tension across the remainder of the healing wound would be markedly altered with consequent changes in healing rate. The unclosed defect, in fact, remained clean and granulated well (*Fig.* 2), and analysis of results from the rest of the wound showed no difference between the properties of specimens cut from areas adjacent to the unclosed defect, and specimens taken from some distance away.

The remaining pigs were utilized to study 5-day incisions. In these animals the linear wounds were 240 mm in length and each contained 16 sutures or clips. For excision purposes these wounds were divided into four equal parts, each containing 4 clips or sutures. Therefore an equal number of wound areas were available for study at 5 days as at the other time periods.

Following excision of each wound area, eight 2-mm wide specimens were cut with a specially fabricated cutter. These specimens had an approximately square cross-sectional area of scar, which is necessary for accurate testing (Glaser et al., 1965). Each specimen was then photographed in both plan and lateral view on a calibrated background using 35-mm colour transparency film. By projection of these views the width and thickness of scar could be very accurately measured and the cross-sectional area calculated—an essential preliminary to the determination of the tensile properties of any specimen.

Specimens, individually wrapped in aluminium foil and suitably labelled for identification, were stored in liquid nitrogen to halt the rapid change in the mechanical properties prior to tensile testing (Marangoni et al., 1966). All specimens in this trial had the same 'warm deterioration' times (18 minutes).

When required for testing each foil-wrapped specimen was thawed in water to room temperature, unwrapped, mounted on the Instron tensile testing apparatus (*Fig.* 3) and tested to failure. An automatic load/extension curve was plotted for each specimen, a total of over 500 being tested in this way. A constant gauge length of 25 mm was used. Because of the fragility of these specimens, especially the 5-day wounds, it was felt that the use of any strain gauge extensometer to measure and control the strain rate would affect the deformational behaviour during the test. It was therefore decided to use a constant extension rate (30 mm/min), accepting that a slight reduction of strain rate would occur during the test because of the constantly increasing length. In this way, all the specimens were subjected to a strain rate that was always within the range shown by Marangoni et al. (1966) to give reproducible results.

If the axes of the load/extension curve obtained from the Instron machine are corrected to those of stress (i.e. load/area) and strain (i.e. extension/original length), then the maximal tensile strength and strain may be read directly. The energy absorbed is represented by the area beneath the curve, and the modulus of elasticity by the slope of the essentially linear part of the curve (*Fig.* 4). The results obtained were statistically analysed by the paired *t*-test and analysis of variance methods.

Table I: TENSILE STRENGTH OF WOUNDS

Time (d)	Sutures	Clips	*P* (paired *t*-test)
5	49 ± 2·3	40 ± 6·5	<0·01
7	85 ± 11	65 ± 7·2	<0·01
15	152 ± 33	91·5 ± 14	<0·01

Mean values and standard deviations in g/mm^2.

Table II: TENSILE STRENGTH OF WOUNDS AT 14 DAYS

	Sutures	Clips	*P* (paired *t*-test)
Early removal	161 ± 28	141 ± 22	>0·05 (n.s.)
Without removal	152 ± 33	91 ± 14	<0·01
P (paired *t*-test)	>0·8 (n.s.)	<0·001	

Mean values and standard deviations in g/mm^2.
n.s., Not significant.

Table III: ENERGY ABSORPTION OF WOUNDS

Time (d)	Sutures	Clips	*P* (paired *t*-test)
5	3·90 ± 0·54	3·25 ± 0·86	>0·5 (n.s.)
7	8·00 ± 1·69	5·77 ± 1·01	<0·01
14	16·51 ± 4·59	9·77 ± 2·43	<0·02

Mean values and standard deviations in g mm mm^{-3}.

Results

Macroscopic appearance

No infection was noted in any wound during the trial. Differences in gross appearance were obvious between nylon-closed and clip-closed wounds. It was seen that a progressive ulceration occurred at the site of contact of clip teeth with skin. This was slight at 5 days, obvious at 7 days (*Fig.* 5) and very gross by 14 days.

Mechanical properties

Tensile strength: Considering first only the wounds in which clips or sutures were retained throughout the healing period, it was seen that at all stages (i.e. 5, 7 and 14 days) wounds closed with nylon sutures had a significantly higher tensile strength than similar wounds within the same animal closed with clips (*Table I*).

Comparison of the strength of 14-day wounds in which clips had been removed after only 7 days showed them to be significantly stronger than similar wounds in which clips had been retained for the entire period. Retention of nylon sutures during the second week of healing produced an insignificant reduction in strength over similar wounds in which sutures were removed early (*Table II*).

Energy absorption: Less energy was required to disrupt clipped wounds than similar nylon-sutured wounds at all stages of healing tested. This difference reached significance level at 7 and 14 days (*Table III*). Comparing 14-day wounds it was seen that considerably more work was required to disrupt wounds from which clips had been removed early than those where clips had been retained for the entire 2 weeks.

Table IV: ENERGY ABSORPTION OF WOUNDS AT 14 DAYS

	Sutures	Clips	*P* (paired *t*-test)
Early removal	15·78 ± 3·29	13·45 ± 1·17	$>$0·05 (n.s.)
Without removal	16·51 ± 4·59	9·77 ± 2·43	$<$0·02
P (paired *t*-test)	$>$0·6 (n.s.)	$<$0·02	

Mean values and standard deviations in g mm mm^{-2}.

Table V: MODULUS OF ELASTICITY OF WOUNDS

Time (d)	Sutures	Clips	*P* (paired *t*-test)
5	380 ± 76	331 ± 68	$>$0·1 (n.s.)
7	592 ± 103	498 ± 56	$>$0·05
14	947 ± 54	531 ± 106	$<$0·001

Mean values and standard deviations in g/mm^2.

Table VI: MODULUS OF ELASTICITY OF WOUNDS AT 14 DAYS

	Sutures	Clips	*P* (paired *t*-test)
Early removal	1045 ± 173	942 ± 222	$>$0·1 (n.s.)
Without removal	947 ± 54	531 ± 106	$<$0·001
P (paired *t*-test)	$>$0·1 (n.s.)	$<$0·01	

Mean values and standard deviations in g/mm^2.

Table VII: TENSILE STRAIN OF WOUNDS

Time (d)	Sutures	Clips	*P* (paired *t*-test)
5	23 ± 1·7	23·5 ± 2·6	$>$0·9 (n.s.)
7	28 ± 3·3	27 ± 1·6	$>$0·4 (n.s.)
14	28 ± 4·2	29 ± 5·4	$>$0·7 (n.s.)

Mean values and standard deviation (%).

Table VIII: TENSILE STRAIN OF WOUNDS AT 14 DAYS

	Sutures	Clips	*P* (paired *t*-test)
Early removal	28 ± 2·9	27 ± 2·9	$>$0·3 (n.s.)
Without removal	28 ± 4·2	29 ± 5·4	$>$0·7 (n.s.)
P (paired *t*-test)	n.s.	$>$0·2 (n.s.)	

Mean values and standard deviations (%).

In the case of nylon-closed wounds the energy absorption for the two groups was virtually identical (*Table IV*).

Modulus of elasticity: The modulus of elasticity was higher for nylon-closed wounds at all stages, this reaching significance level at 7 and 14 days (*Table V*).

Comparing 14-day wounds only, it is seen that the retention of clips throughout the healing period results in a markedly lower modulus than found in wounds where the clips were removed at 7 days. No significant difference was noted between the comparable groups of nylon-closed wounds (*Table VI*).

Tensile strain: No significant difference was noted in the tensile strain between nylon- and clip-closed wounds at any stage of healing. The retention of clips and sutures after the seventh day appeared to make no significant difference to the tensile strains of 14-day wounds (*Tables VII, VIII*).

Discussion

Careful control of the many variables in tensile testing has permitted a statistically valid assessment of the effects of skin clips on wound healing.

The relative importance of the four physical parameters measured is debatable. If a wound could be perfectly elastic, i.e. extend progressively under the influence of an applied force without any increase in tension within the wound, then the tensile strength of the scar would be unimportant. However, since this situation does not obtain and extension leads to progressively increasing tension within the wound, the maximum tensile strength is of vital importance. In the clinical situation all wounds are subjected to various forces tending to rupture them. This results in both extension and increase in tension within the wound, the ratio of these two components being indicated by the modulus of elasticity of that particular wound. Energy is absorbed by the wound as it deforms until saturation occurs, at which time the developed stress exceeds the maximum tensile strength of the scar and rupture occurs. It will be readily seen from this complex interrelationship why descriptions of wounds based upon only one of these parameters may be misleading.

It has been shown that wounds closed with clips are significantly weaker, have a lower modulus of elasticity and are able to absorb less energy than similar wounds in the same animal closed with monofilament nylon sutures. The differences in tensile strength may appear small, being 9 g/mm^2 at 5 days, 19 g/mm^2 at 7 days and 62 g/mm^2 at 14 days. However, if it is remembered that the average thickness of skin is approximately 2 mm, then for a 20-cm long incision (= 400 mm^2 area of scar) the breaking strength of a nylon-closed wound would be greater by 2·8 kg at 5 days, 7·6 kg at 7 days and 24·8 kg at 14 days than a similar wound closed with clips. There appears to be no difference in the tensile strains of the two groups.

It has also been shown that in equivalent groups of 14-day wounds, those in which clips were retained after the seventh day demonstrated markedly poorer tensile properties than similar wounds within the same animal where clips had been removed early. We feel that these results very definitely prove that the presence of skin clips has an adverse effect on wound healing. No comparable differences were noted in the case of nylon-closed wounds, and retention of nylon sutures appears to be without the adverse effect demonstrated by clips.

These results suggest that whilst skin clips have the benefit of speed of application, there are very real drawbacks to their use in areas of the body not normally associated with very rapid healing. In practical terms, this would restrict their use to the head and neck. Very early removal is possible in this region not because collagen synthesis occurs with great rapidity but because wounds are usually under little stress and if the subcutaneous tissues are adequately closed the skin edges will remain in apposition from the time that epidermal union has occurred (usually within 24–36 hours).

Conclusion

The possibility that clips may be removed earlier than conventional sutures because they permit wounds to gain strength more rapidly is shown to be untrue. Indeed, the prolonged retention of clips (in this trial after the seventh day) dramatically slows the gain of tensile strength, modulus of elasticity and energy absorption of skin wounds.

References

ANNIS D. (1973) A sterile 'use-once' clip applicator for skin closure. *Br. J. Surg.* **60**, 686–688.

BECKWITH T. G., BRODY G. S., GLASER A. A., PREVENSLIK T. and WHITE W. C. (1963) Standardisation of methods of measuring the mechanical properties of wounds. *Am. Soc. Mech. Eng.* November 1963, Paper 63–WA–276.

DOUGLAS D. M. (1952) The healing of aponeurotic incisions. *Br. J. Surg.* **40**, 79–84.

FORRESTER J. C. (1973) Mechanical, biochemical and architectural features of surgical repair. *Adv. Biol. Med. Phys.* **14**, 1–34.

GIBSON T., KENEDI R. M. and CRAIK J. G. (1965) The mobile micro-architecture of dermal collagen. A bioengineering study. *Br. J. Surg.* **52**, 764–770.

GLASER A. A., MARANGONI R. D., MUST J. S., BECKWITH T. G., BRODY G. S., WALLER G. R. and WHITE W. C. (1965) Refinements in the method for the measurement of the mechanical properties of unwounded and wounded skin. *Med. Elect. Biol. Eng.* **3**, 411–419.

HARTWELL S. W. (1955) *Mechanisms of Healing in Human Wounds.* Springfield, Ill., Thomas.

MARANGONI R. D., GLASER A. A., MUST J. S., BRODY G. S., BECKWITH T. G., WALLER G. R. and WHITE W. C. (1966) The effect of storage and handling techniques on skin tissue properties. *Ann. NY Acad. Sci.* **136**, 441–453.

SANDBLOM P. (1944) Tensile strength of healing wounds, an experimental study. *Acta Chir. Scand.* (*Suppl.* 89).

Br. J. Surg. Vol. 62 (1975) 950–951

How tight should tension sutures be tied? A controlled clinical trial

I. L. ROSENBERG, T. G. BRENNAN AND G. R. GILES*

SUMMARY

In a prospective randomized trial there was no advantage in tying tension sutures flush with the wound; by tying them loosely (over three fingers of the assistant's hand) there was less wound pain and less cutting in of the tension suture into the ridge of the wound and along the suture tracks.

THERE is an opinion that tension sutures will protect against wound dehiscence (McCallum and Link, 1964), and many surgeons have advocated the routine use of these sutures in the closure of abdominal wounds. It is also true that tension sutures badly placed and tied too tightly will produce a very painful and infected wound and undo whatever advantage is gained in the protection of the wound. The present study has investigated the protection of paramedian wounds by tension sutures tied either loosely or in the usual manner, taking account of wound complications and wound pain.

Patients and methods

One hundred and twenty-eight patients undergoing laparotomy through a new paramedian incision were consecutively entered into a prospective trial; incisions through old scars were excluded from the trial. In all cases the incision was a laterally placed paramedian incision which was closed in layers. The peritoneum and anterior rectus sheath were each closed with continuous No. 1 chromic catgut and the skin with interrupted silk sutures. The tension sutures used were of No. 1 braided polyester coated with polytetrafluoro-ethylene on a 90-mm curved needle with 30-mm retention tubing (Ethicon Ltd). The tension sutures were placed deep to the rectus muscle, superficial to the posterior sheath, passing through all other layers and at intervals of 3–5 cm. The skin entry and exit holes of these sutures were positioned about 2·5 cm from the incision. After randomization, the tension sutures were tied with the loop flush on the skin but not tightly, or loosely with the loop tied over three fingers of the assistant's hand.

Initial wound assessment was conducted on the tenth postoperative day, looking for signs of infection, haematoma, presence of a healing ridge and cutting in of the tension sutures on the ridge or in the needle tracks. An assessment of wound pain was made by the nursing and resident staff and divided empirically into three groups: average, less than average and more than average. Careful note was also taken of the presence of postoperative sputum retention and chest infection. In almost all the patients the skin sutures were removed on the tenth day and the tension sutures on the fourteenth day. In a few cases removal of the tension sutures was delayed where the patient was cachectic or on high dose steroid therapy.

Final assessment was made at least 4 months postoperatively when the wound was examined for the presence or absence of an incisional hernia.

Table I: COMPARISON OF THE TWO GROUPS STUDIED

	Flush tied	Loosely tied
Total	55	58
Male	30	31
Female	25	27
Elective surgery	42	40
Emergency surgery	13	18
Clean laparotomy	13	11
Viscus opened	42	47
Body build		
Thin	22	14
Medium	27	35
Obese	6	9

Table II: SUMMARY OF THE FINDINGS

	Flush tied		Loosely tied		
	No.	%	No.	%	*P*
Burst abdomen	0	0	0	0	
Incisional hernia	1	2	2	3	
Wound pain					
Less than average	17	31	28	48	
Average	30	55	25	43	
More than average	8	15	5	9	
Wound infection	10	18	4	7	>0·05
Haematoma or sero-sanguineous discharge	0	0	5	9	
Normal healing	45	82	49	84	
Infected tension suture	3	5	3	5	
Cutting in along track	33	60	15	26	<0·001
Cutting in on ridge	26	47	10	17	<0·001
Chest infection	12	22	20	34	

Results

Of the 128 patients, 3 died of disseminated malignancy in the early postoperative period and were excluded from the analysis. Thus, the abdominal wounds of 125 patients were assessed on the tenth day; 60 patients had flush tied tension sutures and 65 patients had loosely tied tension sutures.

The two groups appeared well matched for numbers, sex, type of surgery and body build (*Table I*). *Table II* summarizes the findings of the study. It can be seen that there was no significant difference between the groups with regard to the incidence of wound infection, haematoma, serosanguineous discharge, infected tension suture tracks and chest infection. However, as might be expected, loosely tied tension sutures did not usually cut into the ridge of the wound ($P < 0{\cdot}001$) or through the suture holes ($P < 0{\cdot}001$). Wound pain was apparently less in patients with loosely tied sutures but this was not a statistically significant observation.

---

* University Department of Surgery, St James's Hospital, Leeds.

There was no instance of burst abdomen. Fifteen of the patients have been lost to the 4-month post-operative review, but of the 110 patients examined 4 months or more after operation, 3 had an incisional hernia (2 in the loosely tied group).

Discussion

It was not the intention of this study to judge the value of tension sutures in abdominal wound closure. However, the method of closure adopted for the present study appears satisfactory when compared with other reports (McCallum and Link, 1964; Goligher et al., 1975). Tension sutures presumably act by protecting the rectus sheath closure against increased intra-abdominal pressure due to coughing, bowel distension and paralytic ileus.

That abdominal wounds swell during the first week after an operation is a common observation, and flush tied tension sutures become tight and cut into the ridge of the wound and along the suture tracks. This was not the case with loosely tied sutures and the slack in the sutures was taken up by the oedematous wound. Presumably this tightening up of the loosely tied sutures enabled their protective action to continue. Since wound pain appeared lessened by tying the tension sutures loosely and there seemed to be no loss of the protective action of the sutures, when tension sutures are used they should be tied loosely over three fingers of the assistant's hand.

References

GOLIGHER J. C., IRVIN T. T., JOHNSTON D., DE DOMBAL F. T., HILL G. L. and HORROCKS J. (1975) A controlled clinical trial of three methods of closure of laparotomy wounds. *Br. J. Surg.* **62**, 823–829.

MCCALLUM G. T. and LINK R. F. (1964) The effect of closure techniques on abdominal disruption. *Surg. Gynecol. Obstet.* **119**, 75–80.

Br. J. Surg. Vol. 62 (1975) 952–955

Does the choice of suture material affect the incidence of wound infection?

A comparison of Dexon (polyglycolic acid) sutures with other commonly used sutures in an accident and emergency department

G. L. MOUZAS AND A. YEADON*

SUMMARY

One hundred and four patients with superficial lacerations were sutured with either Dexon (polyglycolic acid), silk, polyethylene or nylon sutures. The incidence of postoperative tissue reaction and wound infection was compared.

There were few complications and these occurred with almost the same frequency in each suture group, although there were slightly more cases of infection in the patients who were sutured with silk.

Dexon was seen to possess certain advantages in that it caused as little tissue reaction as the other sutures but did not have to be removed subsequently. This could clearly be of benefit to the patients and hospital staff alike.

THE average casualty surgeon spends a large proportion of his time treating superficial lacerations. Clearly, the efficiency with which this treatment is carried out is of major importance to the patient and hospital service alike.

Although there are many factors related to wound healing that are outside the direct control of the casualty surgeon, there are undoubtedly many ways in which the surgeon and his team can improve the chances of a successful outcome when treating superficial lacerations of the skin. Nichol and Cole (1973) stated that damaged structures should be carefully inspected to ascertain the precise extent of the laceration, which should then be meticulously prepared with débridement of all devitalized tissue. Repair should be carried out skilfully, sutures should not be tied too tightly around the wound edges as this can markedly increase the incidence of infection and good postoperative care is essential to reduce scarring.

The choice of suture material may also be important since the physical and chemical properties of sutures can affect wound healing. Edlich et al. (1973) found that Dexon (a synthetic absorbable suture manufactured from polymerized glycolic acid—PGA) elicited less infection in contaminated subdermal tissues in the mouse than did gut sutures. These workers also stressed the fact that the chemical properties of the suture appeared to be the most important determinant of early postoperative infection, and amongst the absorbable sutures examined in this study PGA appeared to elicit the least inflammatory response in contaminated tissues. Lilly et al. (1973) studied PGA sutures *in vitro* and found that they transmitted bacteria less readily than silk sutures.

In view of these reports and the fact that many lacerations treated in an accident and emergency unit are grossly contaminated, we decided to set up a clinical trial to determine whether the incidence of complications such as tissue reaction and wound infection can be affected by the choice of suture material.

Materials and methods

Four different sutures were studied. These were Dexon, silk, polyethylene and nylon—all sutures which are in common use in accident departments.

Any patient with a skin laceration which did not involve deeper structures was eligible for inclusion in the trial. A careful note was made of the patient's name, age, sex and history. The wound was examined and a note made of its size and extent. The degree of contamination was assessed not only by inspection but also by determining the precise circumstances of the injury and its management before arrival at the hospital. It was recognized, however, that only a very crude assessment of contamination was possible by these means, and as a result wounds were labelled either 'contaminated' or 'uncontaminated'.

Next the lacerations were cleaned and any débridement carried out. As far as possible the choice of suture material was made randomly, although there was a tendency to use Dexon sutures for children since this would avoid suture removal later. Wounds were covered with dry dressings.

All the patients were asked to return for at least two follow-up visits, the first after 2 or 3 days and the second after 7–10 days. At follow-up the wounds were inspected and a note was made of the degree of tissue reaction and infection. If pus was present this was noted and a swab was sent for bacteriological examination. The degree of inflammation was ranked according to the following scale:

0, No reaction, normal healing.

1, Oedema present (this was only recorded if the oedema involved two or more adjacent sutures).

2, Oedema and erythema, probable infection. (Again, erythema was only recorded when it involved two or more sutures. The erythema confined to the needle puncture site was recorded as normal.)

---

* Accident and Emergency Centre, West Hill Hospital, Dartford, Kent, and Davis & Geck, Cyanamid of Great Britain Ltd, Gosport, Hants.

Present address of G. L. Mouzas: Chace Wing, Enfield District Hospital, Middlesex.

3, Oedema, erythema and pus. This was taken as an indication of definite infection and the patient was treated with an antibiotic.

The non-absorbable sutures were removed at the second visit, whereas the Dexon PGA sutures were merely trimmed if necessary. Any patient whose wound was still infected at this stage was asked to return for a further review a week later.

Photographs were taken of some of the typical or interesting cases to allow comparison at a later date.

Results

One hundred and four patients entered the trial. Of these, 71 (68 per cent) were male, with an average age of 32 years (range 2–67 years), and 33 (32 per cent) were female, with an average age of 22 years (range 1–70 years).

The patients in the Dexon group were younger than the mean because there was a tendency to use this material in children since removal was not required. The average age of this group was only 18 years. The average age of the silk group was 30 years, the polyethylene group 26 years and the nylon group 39 years.

Table I shows the number of patients, male and female, who were sutured with each type of material. Contaminated and uncontaminated wounds were fairly evenly represented in the four comparison groups. However, the distribution by sex was not so good since, overall, 68 per cent of the patients were male and 32 per cent were female, and in some subgroups, e.g. patients with contaminated wounds which were sutured with polyethylene, there were 13 males and only 1 female. The split in this group is clearly unrepresentative of the whole.

Table I: DISTRIBUTION OF PATIENTS ON ENTERING THE TRIAL

	Contaminated wounds				Uncontaminated wounds				
Suture used	M	F	Both	%	M	F	Both	%	Total
Dexon	11	4	15	58	6	5	11	42	26
Silk	12	2	14	54	6	6	12	46	26
Polyethylene	13	1	14	61	7	2	9	29	23
Nylon	10	7	17	65	6	6	12	35	29
All suture groups	46	14	60	58	25	19	44	42	104

M, Male; F, Female.

Only 3 patients failed to attend the first follow-up at 2–3 days, one from each of the Dexon, silk and nylon groups. A further 11 patients failed to keep their second follow-up appointment, so that the final number completing the trial was 90. The suture groups contained almost equal numbers of patients at this final assessment.

Table II compares the appearance of the wounds in each suture group after 2–3 days and 7–10 days. The sexes are shown together in the results, since a preliminary analysis of the data indicated no real differences in healing response that could be attributed to sex. Wounds which were classified as contaminated are shown separately from those that were not. In general, the wounds that were originally considered clean showed less tissue reaction and infection than those that were contaminated. For instance, at the first assessment 43 per cent (25 of 58) contaminated wounds looked normal as opposed to 63 per cent (27 of 43) of the clean wounds. By the second assessment at 7–10 days, the difference was less marked: 68 per cent (39 of 57) contaminated wounds looked normal as opposed to 79 per cent (26 of 33) clean wounds. However, these differences are not statistically significant.

Since whether or not the wound was initially thought to be contaminated seemed to have little bearing on the outcome of wound healing, the results shown in *Table II* have been summarized in *Tables III* and *IV*. These tables present the results of contaminated and clean wounds together for each suture group at both assessment stages.

Table II: COMPARISON OF CONTAMINATED AND UNCONTAMINATED WOUNDS IN EACH SUTURE GROUP BY WOUND APPEARANCE AT 2–3 AND 7–10 DAYS

	At 2–3 days			At 7–10 days		
Wound appearance*	Contaminated	Uncontaminated	All wounds	Contaminated	Uncontaminated	All wounds
Dexon						
0	6	6	12	10	7	17
1	5	4	9	3	0	3
2	2	1	3	1	1	2
3	1	0	1	0	0	0
Silk						
0	5	7	12	8	5	13
1	2	2	4	2	2	4
2	3	2	5	1	2	3
3	3	1	4	2	1	3
Polyethylene						
0	6	6	12	9	6	15
1	6	3	9	2	2	4
2	1	0	1	2	0	2
3	1	0	1	1	0	1
Nylon						
0	8	8	16	12	5	17
1	6	2	8	3	2	5
2	2	1	3	1	0	1
3	1	0	1	0	0	0

* *See* text.

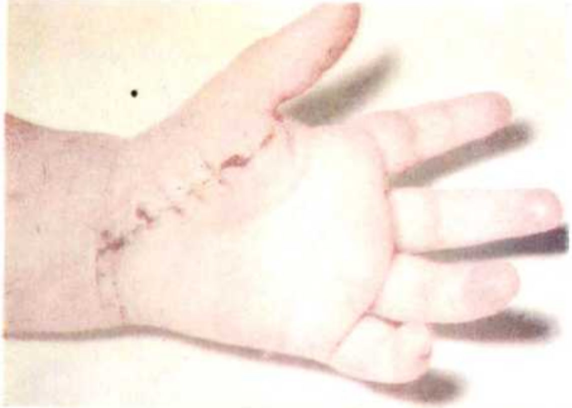


Fig. 1. Dexon in a child with a laceration of the left thenar eminence; there is very little tissue reaction and this was graded as 0.

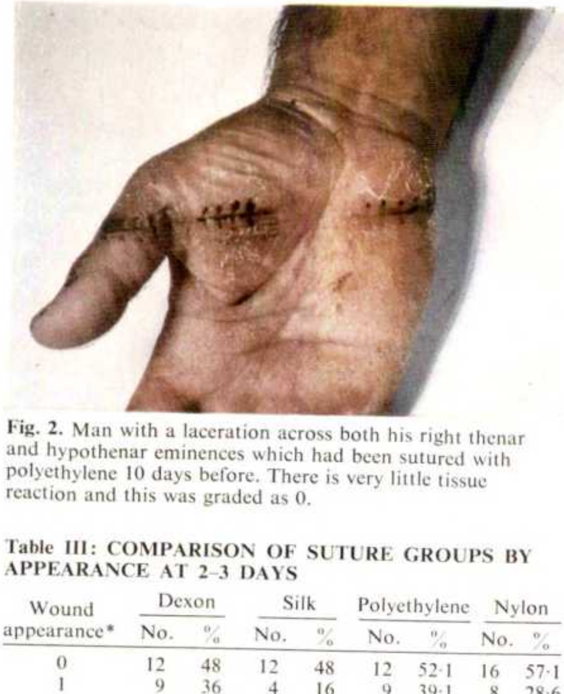


Fig. 2. Man with a laceration across both his right thenar and hypothenar eminences which had been sutured with polyethylene 10 days before. There is very little tissue reaction and this was graded as 0.

Table III: COMPARISON OF SUTURE GROUPS BY APPEARANCE AT 2–3 DAYS

Wound appearance*	Dexon		Silk		Polyethylene		Nylon	
	No.	%	No.	%	No.	%	No.	%
0	12	48	12	48	12	52·1	16	57·1
1	9	36	4	16	9	39·1	8	28·6
2	3	12	5	20	1	4·4	3	10·7
3	1	4	4	16	1	4·4	1	3·6
Total	25		25		23		28	

* *See* text.

Table IV: COMPARISON OF SUTURE GROUPS BY APPEARANCE AT 7–10 DAYS

Wound appearance*	Dexon		Silk		Polyethylene		Nylon	
	No.	%	No.	%	No.	%	No.	%
0	17	77·3	13	56·5	15	68·2	17	73·9
1	3	13·6	4	17·5	4	18·2	5	21·7
2	2	9·1	3	13·0	2	9·1	1	4·4
3	0		3	13·0	1	4·5	0	
Total	22		23		22		23	

* *See* text.

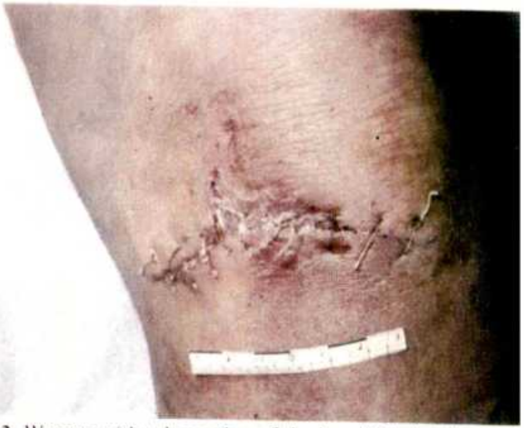


Fig. 3. Woman with a laceration of the leg which had been sutured with Dexon 10 days before. There is some oedema present at either end of the wound. This was graded as 1.

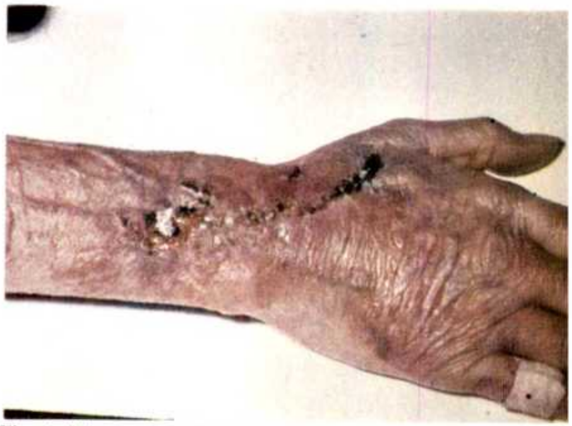


Fig. 4. Elderly man with a severe and contaminated laceration of the hand and forearm which had been sutured with silk. Oedema, erythema and pus are all present.

At 2–3 days there was very little difference between the number of wounds that appeared normal in each suture group, but whereas only 1 wound in each of the Dexon, polyethylene and nylon groups was frankly infected, 4 of the wounds sutured with silk were infected. These 7 patients were given antibiotics after a swab had been taken.

By 7–10 days 77·3 per cent (17 of 22) of the Dexon wounds, 68·2 per cent (15 of 22) of the polyethylene wounds and 73·9 per cent (17 of 23) of the nylon wounds were normal in appearance, whereas only 56·5 per cent (13 of 23) of the silk sutured wounds were considered normal. This difference, although interesting, is not statistically significant ($\chi^2 = 1{\cdot}7858$, d.f. = 3, $0{\cdot}70 > P > 0{\cdot}50$).

Four wounds were still infected at the second assessment—3 in the group sutured with silk and 1 in the polyethylene group. The antibiotic was changed in 2 of these and all were improving when they were seen a week later.

Figs. 1–4 give some indication of the type of reactions observed.

Conclusions

In this study an attempt was made to examine the degree to which the choice of suture material could affect the incidence of tissue reaction and wound infection in superficial lacerations.

It was interesting that the degree of initial wound contamination did not appear to affect the incidence of infection significantly. This may have been due to the fact that only relatively small numbers of patients were examined or that the criteria for judging a wound contaminated or not were insensitive.

When all the results are taken together (*Tables III* and *IV*) there appear to be no significant differences in the incidence of tissue reaction between the four sutures examined. There was a tendency, however, for more silk wounds to become infected. This was true at 2–3 days and 7–10 days. Synthetic non-absorbable sutures such as nylon are well known for their inertness. In this study Dexon, a new synthetic absorbable suture, performed as well as the non-absorbable materials, causing as little trouble as nylon and polyethylene, and fewer cases of tissue reaction and infection than silk.

On the basis of these findings it would seem that Dexon sutures have certain advantages over the other sutures tested, in that, whilst they perform just as well, they could save the medical and nursing staff time, the Hospital Service money and the patients the trouble of follow-up visits for suture removal.

References

EDLICH R. F., PANEK P. H., RODEHEAVER G. T., TURNBULL V. G., KURTZ L. D. and EDGERTON M. T. (1973) Physical and chemical configuration of sutures in the deveoplment of surgical infection. *Ann. Surg.* **177**, 679–688.

LILLY G. E., OBSON D. B., HUTCHINSON R. A. and HEFLICH R. H. (1973) Clinical and bacteriologic aspect of polyglycolic acid sutures. *J. Oral Surg.* **31**, 103–105.

NICHOL T. D. and COLE N. M. (1973) Management of soft tissue injuries of the face to reduce scar formation. *J. Ky Med. Assoc.* **71**, 495–499.

Br. J. Surg. Vol. 62 (1975) 956

Gangrene of the tongue following self-application of a rubber band

T. DUTTA AND K. VASUDEVAN*

SUMMARY

A case of dry gangrene of the tongue due to self-application of an elastic rubber band in a mentally retarded child is described. As far as is known, no such case of gangrene of the tongue has been described in the English literature.

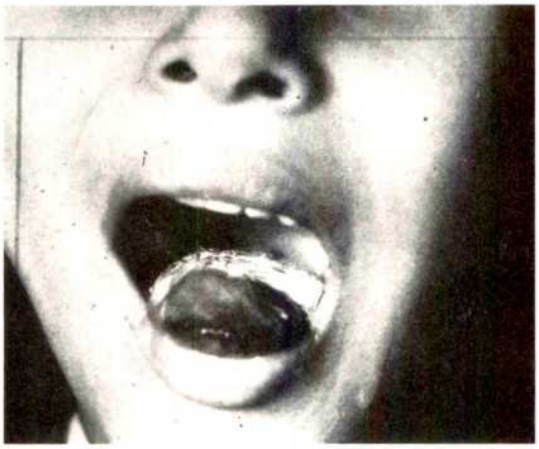


Fig. 1. Tongue on presentation showing gangrene of its anterior third.

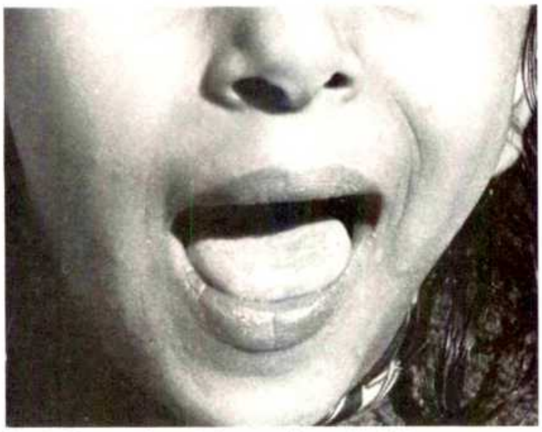


Fig. 2. Tongue 4 weeks later, with no disability.

GANGRENE of the tongue is extremely rare. The tongue is one of the most vascular organs in the body and any vascular insult is quickly overcome by the rich blood supply.

Case report

M. K., an 8-year-old female child, was examined in the children's surgical outpatients' department of Safdarjang Hospital, New Delhi, in October 1974, because of a 'black patch on the tongue' which had been present for 3 days. Two days earlier the parents had noticed that the child had difficulty in speaking and eating food, and the tongue was swollen and discoloured.

Examination revealed a frail mentally retarded child. Systemic examination was normal. Local examination revealed a distinct groove of 0·5 cm depth at the junction of the middle and anterior thirds of the tongue beyond which the tongue was black and shrivelled (*Fig.* 1). At the bottom of the groove there was a stretched rubber band which was the cause of the strangulation of the distal third of the tongue. The child confessed that she had applied the rubber band 3 days earlier. Her parents had not noticed it.

The distal one-third of the tongue which was gangrenous had no sensation and did not bleed on pricking. The proximal two-thirds of the tongue were normal. The child's speech was indistinct (dyslalia), and she was unable to stick out her tongue.

The rubber band was removed immediately and oral penicillin administered.

The gangrenous part of the tongue withered and fell off 3 days later without any bleeding. The child was seen in the surgical follow-up clinic 4 weeks later and was apparently having no difficulty in speech or deglutition. The tip of the tongue was smooth and rounded and had normal mobility (*Fig.* 2).

Discussion

The whole episode was of short duration and the gangrenous part of the tongue separated off rather quickly because of the rich vascularity of the tongue, and perhaps also because the necrosis may have been mainly confined to the mucosa and submucosal layers, as in ring strangulation of the penis. There were no later complications. A search of the literature has failed to reveal any similar report of gangrene of the tongue.

Acknowledgement

Our thanks are due to Brigadier S. Gopalakrishnan for permission to publish this case report.

---

* Safdarjang Hospital, New Delhi-110016, India.

DISPRAY 1
Trade Mark
Quick Prep
Chlorhexidine gluconate 0.5% w/v in 70% I.M.S.
Stuart Pharmaceuticals Limited Cheadle, Cheshire
DISPRAY 2
Hard Surface Disinfectant
Chlorhexidine gluconate 0.02% w/v in 70% I.M.S.
Stuart Pharmaceuticals Ltd Cheadle, Cheshire

DISPRAY 1
TRADE MARK
Quick Prep
Chlorhexidine Gluconate 0.5% w/v
in 70% Industrial Methylated Spirit.

The pick of the bunch for skin disinfection

'Dispray' 1 Quick Prep. (formerly known as Hibispray 1) is an ideal preparation for skin and hand disinfection in the busy hospital environment.

At the touch of a button it gives fast, easy and economical skin disinfection prior to surgery, injection or venepuncture.

When colour delineation is required eg. pre-operatively, 'Dispray' 3 is available with a red dye.

The 'Dispray' range combines effectiveness with convenience and economy.

Instant Availability.
No solutions to prepare.

Easy to use.
No swabs or bottles required.

Quick and Effective.
Rapid bactericidal action.

Efficient Application.
No wasted solutions.

Contents cannot be contaminated.
No rejected solutions.

Long Lasting.
Contents of one can treat 100 sq. ft.

'Dispray' 1, 2, 3.
The Pick of the Bunch for Disinfection.

DISPRAY 2
TRADE MARK
Hard Surface Disinfectant
Chlorhexidine Gluconate 0.02% w/v
in 70% Industrial Methylated Spirit.

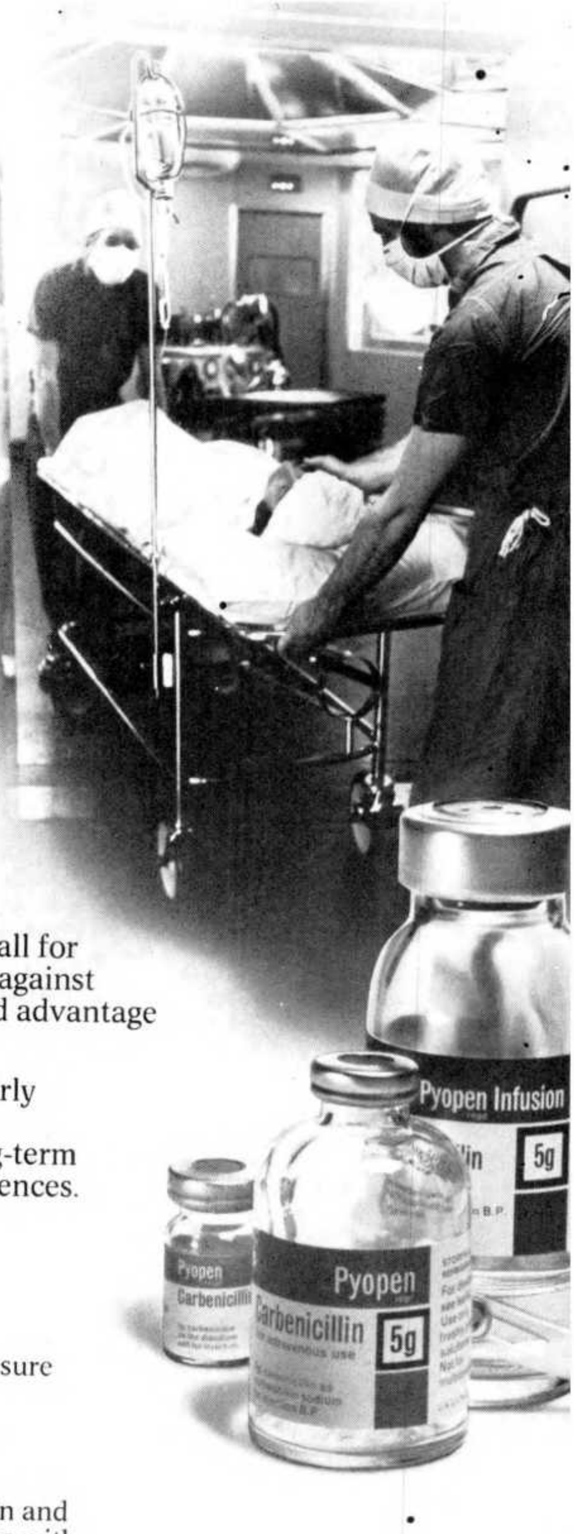
The pick of the bunch for hard surface disinfection

'Dispray' 2 Hard Surface Disinfectant (formerly known as Hibispray 2) provides rapid disinfection of all hard surfaces throughout the hospital. Trolleys, cabinets, cupboards, working surfaces – even footwear, are rapidly, effectively and efficiently disinfected.

Further information is available from:

STUART

Stuart
Pharmaceuticals
Limited,
Carr House,
Carrs Road,
Cheadle,
Cheshire SK8 2EG.



When pseudomonas threatens...

Pyopen

The skill of the surgical team,
hours in the theatre, the most advanced
techniques in the world . . . and infection
can still throw the outcome into jeopardy.

Systemic pseudomonas or proteus infections call for Pyopen. Only Pyopen offers you good activity against these Gram-negative organisms with the added advantage of penicillin safety.

Intravenous Pyopen, at a dosage of 5g 4–6 hourly will rapidly control many of these dangerous infections. And Pyopen is also suitable for long-term therapy and for patients with lowered host defences.

Adult Dosage
5g I.V. 4–6 hourly.
In patients with renal impairment dosage may be reduced; monitoring is advisable in these cases to ensure adequate serum antibiotic levels.
Contra-indication
Penicillin hypersensitivity.
Side-effects
As with other injectable penicillins. In rare cases, skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Pyopen – by infusion or injection

Further information is available on request.
Pyopen* (carbenicillin sodium B.P.) is a British product originated by
Beecham Research Laboratories, Brentford, England. *regd.

Br. J. Surg. Vol. 62 (1975) 957–962

In situ intraduct carcinoma of the breast: a long term follow-up study

R. R. MILLIS AND G. S. J. THYNNE*

SUMMARY

Twenty-eight patients with in situ intraduct carcinoma of the breast are reviewed. Two patients had bilateral tumours. The numbers of patients treated by wide local excision, simple mastectomy and mastectomy with axillary dissection were approximately equal; none of these patients died of carcinoma. The conclusions regarding prognosis and treatment of in situ intraduct carcinoma of the breast are discussed.

THIS study of 28 cases of intraduct carcinoma diagnosed at the Royal Marsden Hospital between 1948 and 1968 has been undertaken to determine the natural history of this condition.

Intraduct carcinoma frequently contains microcalcification which is often detectable by radiological examination of the breast before a mass can be felt or seen on an X-ray. Radiological examination is now used in conjunction with other methods of examination for the earlier diagnosis of breast cancer, in particular in the screening clinics recently established. The early manifestations of breast carcinoma include *in situ* lobular carcinoma and *in situ* duct carcinoma. Much is known about the long term results in patients with *in situ* lobular carcinoma (McDivitt et al., 1967; Hutter and Foote, 1969; Haagensen, 1971; Anderson, 1974; Wheeler et al., 1974), but fewer groups of patients with *in situ* duct carcinoma have been studied (Gillis et al., 1960; Farrow, 1970; Ashikari et al., 1971).

Materials and methods

All histological reports of carcinoma of the breast made in the Royal Marsden Hospital Pathology Department between 1948 and 1968 have been studied, and relevant sections of cases in which the diagnosis may have been *in situ* duct carcinoma have been reviewed. Extremely strict histological criteria have been applied and only those in which a histological diagnosis of *in situ* intraduct carcinoma can now be made with certainty have been included. Haematoxylin and eosin sections have been examined, new sections being prepared, as well as a section stained for elastic and other special stains when indicated. The following cases were excluded: those in which the biopsy was small, such as a drill biopsy where it is not possible to be certain that the material is representative; those in which only slides referred from another hospital for a second opinion were available; those in which there was any suggestion of invasion, either in the original slides or in recuts from the blocks. Cases with Paget's disease associated with underlying *in situ* intraduct carcinoma have also been excluded, since there is still much debate concerning the source of the malignant intra-epidermal cells. One patient excluded gave a history of removal of the other breast for invasive carcinoma a few years previously. Three cases of intracystic carcinoma have been included in the study (McDivitt et al., 1968).

From a review of 85 cases, a total of 28 patients with *in situ* intraduct carcinoma have been considered acceptable for detailed study. Two patients had bilateral tumours (i.e. 30 tumours). Seventeen of the cases were diagnosed between 1948 and 1963 and 11 between 1964 and 1968.

Results

The details of the history, clinical findings, treatment and follow-up are shown in *Table I*.

Age distribution and menopausal status

The age and menopausal status of the patients at the time at which the diagnosis was made are shown in *Table II*, the patients being grouped by decades. The mean age was 55 years and the range 39–84 years.

Family history

The family history had not been recorded in 11 cases. A family history of carcinoma of the breast was present for 7 of the 17 patients for whom this information had been recorded. Two of these 7 patients had, in addition, a family history of carcinoma in sites other than the breast, and 2 other patients gave a family history of carcinoma at another site.

Marital status, parity and breast feeding

Eighteen patients were married and 10 single. The 10 single patients were nulliparous. Of the 18 married women, 6 had had 1 child, 7 were multiparous and parity was unrecorded in the other 5 patients. Breast feeding was not recorded with sufficient frequency to permit adequate analysis. None of the patients had presented during pregnancy or lactation.

Clinical presentation

Twenty-four patients presented with a clinical mass, 2 of whom had bilateral masses. Six of these patients also gave a history of pain and 5 a history of nipple discharge, which was bloodstained in 2 cases. Discharge or bleeding from the nipple was the only abnormality found in 3 patients. One patient's only complaint was of pain in the breast.

Table III gives the size of the palpable mass at the time of presentation.

---

* Breast Unit and Departments of Pathology and Surgery, Royal Marsden Hospital, London.

Table I: DETAILS OF THE PRESENT SERIES

Case	Age	Parity	Menopausal status	Relevant family history of breast cancer	Duration of symptoms	Presenting symptoms	Clinical findings	Treatment	Pathology	Recurrence	Length of follow-up	Present state of health
1	47	0	Menopausal	NR	3 mth	Lump and nipple bleeding	6-cm mass	Radical mastectomy	Comedo		15 yr and over	Lost to follow-up at 19 yr, when alive and well
2	59	0	Postmenopausal	NR	2 wk	Lump	Mass, size NR	Radical mastectomy	Cribriform			Alive and well
3	45	2	Post-hysterectomy	NR	6 wk	Lump and pain	5-cm mass	Radical mastectomy	Comedo			Alive and well
4	55	1	Postmenopausal	NR	3 wk	Lump	3-cm mass	Simple mastectomy and postoperative radiotherapy	Comedo			Alive and well
5	58	1	Postmenopausal	Yes	4 mth	Nipple discharge	2-cm mass	Simple mastectomy	Mixed			Alive and well
6	40	NR	Premenopausal	Nil	18 mth	Lump	2·5-cm mass	Wide local excision	Comedo	At 6 mth, radical mastectomy and postoperative radiotherapy		Alive and well
7	45	3	Premenopausal	Yes	3 yr	Lump	Nodularity	Wide local excision	Low papillary			Alive and well
8	46	0	Menopausal	Nil	5 wk	Lump	1·5-cm mass	Radical mastectomy, preoperative radiotherapy	Cribriform			Lost to follow-up at 17 yr, when alive and well
9	49	2	Post-hysterectomy	Nil	2 mth	Left: lump	Left: 1-cm mass	Left: wide local excision	Comedo			Alive and well
						Right: lump and pain	Right: mass, size NR, and enlarged axillary nodes	Right: radical mastectomy	Cribriform			
10	44	NR	Premenopausal	NR	6 wk	Lump	Small mass	Simple mastectomy	Comedo			Alive and well
11	40	0	Premenopausal	Nil	2 wk	Lump and pain	7·5-cm mass	Simple mastectomy	Cribriform			Alive and well
12	79	1	Postmenopausal	Nil	1 wk	Lump and nipple discharge	9-cm mass and discharge	Simple mastectomy	Comedo		10–14 yr	Died of cerebrovascular accident at 13 yr. No clinical recurrence
13	70	2	Postmenopausal	Yes	NR	Nipple bleeding	Nipple bleeding	Wide local excision	Cribriform			Alive and well
14	47	NR	Menopausal	NR	2 wk	Lump	Mass, size NR	Radical mastectomy	Comedo			Died of cerebrovascular accident at 14 yr. No clinical recurrence.
15	39	3	Premenopausal	Nil	1 mth	Lump and pain	1-cm mass	Radical mastectomy	Comedo			Alive and well
16	86	1	Postmenopausal	NR	2 wk	Lump	Mass, size NR	Wide local excision	Intracystic		5–9 yr	Died of congestive cardiac failure at 6 yr. No clinical recurrence
17	56	NR	Postmenopausal	Yes	3 mth	Lump	2-cm mass	Extended simple mastectomy	Comedo			Alive and well
18	72	NR	Postmenopausal	NR	3 mth	Nipple discharge	Discharge	Extended simple mastectomy	Cribriform			Alive and well
19	45	0	Premenopausal	NR	1 wk	Lump and pain	5-cm mass	Wide local excision	Low papillary			Alive and well
20	43	0	Premenopausal	Nil	3 wk	Pain	4-cm mass	Simple mastectomy	Cribriform			Alive and well
21	64	1	Postmenopausal	NR	1 mth	Lump	2-cm mass	Wide local excision	Intracystic			Alive and well
22	63	0	Postmenopausal	Yes	3 wk	Lump, pain and nipple bleeding and discharge	2-cm mass	Radiotherapy	Mixed	At 6 yr increase in size of mass and skin ulceration		Died at 7 yr with congestive cardiac failure and metastatic carcinoma of breast
23	51	0	Postmenopausal	Yes	1 yr	Lump and nipple discharge	Mass, size NR and discharge	Simple mastectomy	Comedo			Alive and well
24	42	3	Premenopausal	Nil	1 mth	Lump	1·5-cm mass	Wide local excision	Low papillary	At 7 yr + At 8 yr→simple mastectomy		Alive and well
25	63	0	Postmenopausal	Yes	2 mth	Lump	Mass, size NR	Simple mastectomy	Low papillary		Less than 5 yr	Died of congestive cardiac failure at 4 yr. No clinical recurrence
26	67	0	Postmenopausal	Nil	1 wk	Lump and discharge	7-cm mass	Wide local excision, postoperative radiotherapy	Low papillary			Died of coronary thrombosis at 2 yr. No clinical recurrence
27	42	1	Premenopausal	NR	6 mth	Lump	9-cm mass and enlarged axillary nodes	Extended simple mastectomy	Comedo			Lost to follow-up immediately postoperatively
28	84	>5	Postmenopausal	Nil	5 yr	Left: lump	9-cm mass and enlarged axillary nodes	Bilateral simple mastectomy	Left: cribriform			Died immediately postoperatively
					2 mth	Right: lump and nipple discharge	5-cm mass		Right: intracystic			

NR, Not recorded.

In 11 patients axillary lymph nodes were palpable, and in 3 these were thought to be significant.

Duration of symptoms

The duration of symptoms before presentation was less than 3 months in over half the patients and over a year in only 3 cases. One patient gave a history of a mass for 5 years. For 1 patient the duration of the presenting symptom was not recorded.

Treatment

Table IV lists the initial treatment given to each patient. Over half the patients were treated by wide local excision or simple mastectomy.

In 3 of the 9 patients treated by wide local excision a diagnosis of *in situ* intraduct carcinoma was made by frozen section. In 1 case the frozen section was negative, and in 5 patients a frozen section was not requested.

Four surgeons were associated with the treatment of the patients in this series. Two did not perform a radical mastectomy for this disease. The other 2 surgeons practised various operations, tending to reserve wide local excision for patients who had had a previous contralateral mastectomy, for the elderly and for those with severe systemic disease, thus performing a radical mastectomy only on the younger patients of the series. One patient with severe cardiac asthma was treated by radiotherapy alone.

Table II: AGE AND MENOPAUSAL STATUS OF PATIENTS

Age (yr)	No. of cases	Menopausal status
31–40	3	All premenopausal
41–50	11	6 premenopausal 3 menopausal 2 post-hysterectomy
51–60	5	All postmenopausal
61–70	5	All postmenopausal
71–80	2	All postmenopausal
81 and over	2	All postmenopausal
Total	28	

Table III: CLINICAL SIZE OF MASS ON PRESENTATION

Size of mass (cm):	No. of cases:
>5	6
2–5	10
<2	5
No mass	3
Not recorded	6
Total	30

Table IV: TREATMENT

Treatment:	No. of cases:
Wide local excision	9
Simple mastectomy	10
Extended simple mastectomy	3
Radical mastectomy	7
Radiotherapy only	1
Total	30
Radiotherapy preoperatively	1
Radiotherapy postoperatively	2

Radiotherapy was given preoperatively to 1 patient treated by radical mastectomy. Postoperative radiotherapy was given to 1 case treated by a simple mastectomy and to 1 treated by wide local excision.

There were 2 patients with bilateral intraduct carcinomas of the breast. One was treated by wide local excision on one side but had radical mastectomy on the other side because of clinically significant ipsilateral lymph nodes. The other patient, who died in the immediate postoperative period, had bilateral simple mastectomies.

Follow-up

One patient who was a poor operative risk (84 years old with hypertension) developed cardiac arrhythmia and died in the immediate postoperative period. One patient returned abroad immediately after operation and has not been followed up since at the Royal Marsden Hospital.

The patient treated by radiotherapy alone died at 7 years with skeletal metastases.

Of the other 25 patients, 3 died before the 10-year follow-up, and 2 between 10 and 14 years after operation (*Table V*). All 5 patients died of other causes, without clinical signs of recurrence. Two patients were lost to follow-up after 15 years but were alive and well without recurrence when last seen.

The remaining 18 cases are still being followed up and are at present alive and well. Eleven have been followed up for over 10 years and 7 for over 5 years. Two in the latter group had recurrences.

Recurrence and metastases

In 2 patients there was local recurrence after initial treatment by wide local excision. In one this occurred 6 months postoperatively and was treated by radical mastectomy. In the other patient a recurrence at 7 years was also treated by wide local excision, but a second recurrence at 8 years was treated by simple mastectomy. Both patients are still alive with no further sign of disease.

The patient who succumbed with known skeletal deposits died 7 years after treatment by radiotherapy only.

Table V: FOLLOW-UP

Length of follow-up	Alive and well	Lost to follow-up	Died with metastatic carcinoma	Died with no evidence of metastatic carcinoma	Total
15 yr and over	9	2	0	0	11
10–14 yr	2	0	0	2	4
5–9 yr	7	0	1	1	9
Less than 5 yr	0	1	0	3	4
Total	18	3	1	6	28

Table VI: HISTOLOGICAL FEATURES

Histological pattern	No. of cases
Comedo	12
Cribriform	8
Lining and low papillary	5
Mixed	2
Intracystic	3
Total	30

Table VII: NUCLEAR PLEOMORPHISM AND MITOTIC RATE

Nuclear pleomorphism	No. of cases
Mild	5
Moderate	13
Marked	12
Total	30

Mitotic figures	No. of cases
Few	15
Moderate	10
Frequent	5
Total	30

Pathological features

A total of 30 tumours from 28 patients have been studied. In many of the earlier cases the macroscopic description was brief and sometimes not very clear. However, the most common features mentioned were prominent or cystic ducts, sometimes associated with a firm area. Creamy exudate was described in the cases of typical comedocarcinoma. In other cases an ill-defined firm area was the only abnormality noted. A cyst was described in the 3 cases of intracystic tumour. No abnormality was remarked upon in 5 cases, and the gross appearance was not described in 3.

Size

The size of the lesion had not always been recorded in the gross description and it was often not possible to determine whether the lesion had been multifocal. However, judging from the size of the lesion sectioned, 6 cases appear to have involved less than 1 cm of breast tissue, 9 cases probably extended from 1 to 2 cm and in 15 cases the lesion involved more than 2 cm of breast tissue. There appeared to be no correlation between the size of the pathological lesion and the clinical presence of a mass, or with the clinical size of mass where this was recorded.

Histology

A summary of the histological features of the tumours can be seen in *Tables VI* and *VII* (McDivitt et al., 1968).

Pattern: The pattern of the lesion within the ducts was in most cases varied and mixed, with a single or multiple layer of malignant cells lining the duct. Frequently, the whole lumen was occluded by malignant cells, usually with necrosis of the central area producing the typical comedo pattern, and this pattern was seen alone or predominated in 12 cases. In 5 cases a thin layer of lining cells, often with a low papillary pattern, was present; in 8 cases there was a predominant cribriform pattern, and in 2 cases a mixture of patterns. In all these cases multiple ducts were involved. Three patients had intracystic papillary carcinoma. In 2 of these the lesion was markedly papillary with fairly well-developed fibrovascular stalks; in the other the tumour was more solid with supporting stalks poorly developed or absent. In none of these cases was the cyst wall invaded.

In patients who presented with a nipple discharge or bleeding all types of histological pattern were seen. One of these patients had an intracystic papillary carcinoma.

Nuclear features: Nuclear pleomorphism was variable and most marked in the typical comedocarcinomas where giant cells were numerous. However, marked pleomorphism and occasional giant cells were also present in some of the lesions in which there was only a thin layer of malignant cells lining the ducts. The mitotic rate was also variable and was often highest in patients with a comedo pattern where there was also marked nuclear pleomorphism. The intracystic carcinomas showed varying degrees of nuclear pleomorphism, but in none was the mitotic rate high.

Other features: Necrosis was present to a variable degree in most of the lesions, and was especially prominent in comedocarcinomas. Calcification was present in 10 cases and was usually found in the area of central necrosis in the comedocarcinomas. It was not found in this series in any of the 3 intracystic carcinomas. In 1 case calcification was localized within dilated adjacent non-malignant ducts. Mucin secretion was evident in the haematoxylin and eosin sections in over half the tumours, but was not a prominent feature. In 1 intracystic carcinoma mucin secretion was prominent and surrounded the papillary fronds.

Lymphocytic infiltrate around the malignant ducts was variable and was only prominent in 4 comedocarcinomas. Condensation of the stroma was sometimes seen around malignant ducts, but even with the use of Weigert's elastic stain elastosis was not demonstrated.

Dysplasia, most commonly fibrocystic disease, was seen in the surrounding tissues in over half the cases.

Lymph nodes from all the cases treated by radical mastectomy, including the 3 patients with significant clinical nodes, were free of metastatic carcinoma.

Nuclear pleomorphism was prominent in the lesion from the patient who died with metastatic carcinoma and in the lesions from the 2 patients with local recurrence, but in none was the mitotic rate high. In the patient who had two local recurrences the histological pattern showed a thin layer of malignant cells lining the duct, sometimes producing a low papillary pattern with marked nuclear pleomorphism but few mitoses. Both recurrences showed the same pattern. In the other patient with a recurrence a comedo pattern was present on both occasions. Tissue from the patient who died showed a mixed pattern but was insufficient for further comment. Since it was an incisional biopsy it could well have represented intraduct carcinoma around the edge of an infiltrating carcinoma.

Simultaneous bilateral carcinomas were present in 2 patients. One patient had a cribriform pattern on one side and an intracystic papillary carcinoma on the other. This patient died in the immediate postoperative period. In the other patient the malignant ducts showed a comedo pattern on one side and a cribriform pattern on the other.

Discussion

The small number of cases in this review, found over a period of 20 years, indicates a low incidence of diagnosis of this disease without accompanying infiltration. The numbers compare well with the study by Gillis et al. (1960), from the Mayo clinic, who found 36 cases of pre-invasive intraduct carcinoma after a study of 603 cases diagnosed as comedocarcinoma from 1928 to 1955. Figures from the Memorial Hospital, New York (Farrow, 1970), indicated an overall incidence of *in situ* carcinoma of the breast of 12 per cent, of which 30 per cent were the *in situ* intraduct type, i.e. approximately 4 per cent of all the breast carcinomas diagnosed. Their figures also showed an increase in the diagnosis of non-infiltrating mammary carcinoma during the 19 years preceding 1970. Another more recent report from the same centre (Ashikari et al., 1971) described 143 patients with intraduct carcinoma during the 10-year period 1960–9.

Some authors have suggested that the low incidence of intraduct carcinoma may be an indication of the aggressive nature of this lesion, i.e. it rapidly becomes invasive and progressive (Gillis et al., 1960; Somers, 1969). However, the good survival in the long term follow-up in the present series, and the fact that the 2 recurrent cases both remained *in situ*, does not support this view, and suggests, on the contrary, that these tumours do not have an aggressive behaviour.

There have been no controlled studies to confirm that untreated cases of *in situ* intraduct carcinoma eventually progress to invasion. However, several studies carried out have demonstrated the multifocal nature of this disease. That 2 out of 6 cases treated by wide local excision recurred and that 2 patients had bilateral *in situ* carcinoma tend to support this, and lend emphasis to the need for a diligent search for a second carcinoma. With increasing use of radiological examination of the breast, more cases of *in situ* intraduct carcinoma are being detected by the presence of micro-calcification before a mass is palpable. Is this because more cases of ductal carcinoma are being detected earlier or because more cases of a separate disease which remains *in situ* for a long time are being detected by this new method of investigation?

In this series a lump in the breast was the major presenting symptom. Pain and nipple discharge were also common. Each occurred as the only symptom in 1 case. (This underlines the need to investigate patients who present with these symptoms alone.)

Over half the patients presented within 6 months of the onset of symptoms. The patient who had felt a mass 5 years before presentation had bilateral tumours, was 84 years old and died in the early postoperative period. The 2 patients who presented at 3 years and 18 months after the onset of symptoms are still alive after 16 years and 26 years respectively.

The higher incidence of carcinoma of the breast in nulliparous women and those with a strong family history is again shown in this study.

The histological classification of non-infiltrating intraduct carcinomas differs at different centres. Muir (1941) recognized incipient duct carcinoma as lesions in which there were heaped-up papillae, a cribriform network or multiple solid foci. Haagensen (1971) divided intraduct carcinoma into four types: comedo, solid, cribriform and low papillary, and considered that approximately 15 per cent of carcinomas of the breast were of this type. McDivitt et al. (1968) described three types of non-infiltrating duct tumours, namely non-infiltrating papillary carcinoma (cribriform), non-infiltrating solid or comedocarcinoma and intracystic carcinoma.

Somers (1969) suggested that the degree of nuclear differentiation in *in situ* intraduct carcinoma is higher than in infiltrating carcinoma, reflecting the enhanced invasive capacity of less differentiated mammary carcinoma cells. Similarly, Gillis et al. (1960) thought that the malignant process began as a proliferation of cells lining ducts producing an ingrowth, often papillary, of well-differentiated cells with few mitotic figures. This process progressed to a more solid intraduct tumour coalescing to produce a cribriform pattern, and eventually forming a solid mass of cells with a progressive increase in anaplasia and mitotic activity.

There have been reports (Muir, 1941; Ashikari et al., 1971) of metastases in axillary nodes in cases of *in situ* intraduct carcinoma where no actual infiltration of the stroma of the breast could be demonstrated. In whole organ studies, Gallagher and Martin (1969) found lymph node metastases in 2 cases where only intraduct lesions could be found in the breast. Studies using the electron microscope have indicated that invasion is present in most cases presumed to be non-infiltrating by light microscopic examination (Ozzello, 1971).

The need for extensive studies of multiple blocks and multiple levels to exclude evidence of small foci of stromal invasion is well recognized, and because of the extreme diffculty of determining the absence of such foci some authors hesitate to recommend anything less than radical mastectomy as curative (Gillis et al., 1960; Farrow, 1970; Ashikari et al., 1971). However, Silverberg and Chitale (1973), in a study to assess the significance of proportions of intraductal and infiltrating tumour growth, found after a study of their series and a review of the literature 'that women with pure intraduct carcinoma (which should be diagnosed only after multiple permanent sections) can safely be treated by less than radical mastectomy and should have virtually normal life expectancies after treatment'. The present series supports this contention.

Conclusion

The numbers in the present series are too small to draw any firm conclusions as to the best treatment, but do support the relatively favourable prognosis in this type of breast carcinoma.

There was no difference in survival between patients treated by wide local excision or simple mastectomy and those treated by radical surgery. In 2 cases local recurrence after wide local excision was treated by more radical surgery. Neither of these patients has died of the disease.

It would seem justifiable to treat young patients (under 35 years), where radical therapy is less acceptable, and older patients (over 70 years) by wide local excision and careful follow-up at regular intervals.

Patients between 35 and 70 years are probably best treated by mastectomy and low axillary node dissection.

Even if the electron microscopic studies are correct, and all intraduct carcinomas are invasive from inception, there does appear to be a group of cases which behave much less aggressively than obvious invasive carcinoma. This emphasizes the value of the current work on the early detection of breast carcinoma.

Acknowledgements

We would like to thank Dr I. M. E. Hamlin and Mr W. P. Greening for their advice and encouragement. We are also grateful to the histopathology technicians for their help and to Miss M. E. Craddock for preparing the typescript. Both authors hold a research grant from the Eranda Trust of the Breast Unit, Royal Marsden Hospital.

References

ANDERSON J. A. (1974) Lobular carcinoma in-situ. *Acta Pathol. Microbiol. Scand.* **82**, 519–533.

ASHIKARI R., HAJDU S. I. and ROBBENS G. F. (1971) Intraductal carcinoma of the breast. *Cancer* **28**, 1182–1187.

FARROW J. H. (1970) Current concepts in the detection and treatment of the early breast carcinomas. *Cancer* **25**, 468–477.

GALLAGHER H. S. and MARTIN J. E. (1969) Early phases in the development of breast cancer. *Cancer* **24**, 1170–1178.

GILLIS D. A., DOCKERTY M. B. and CLAGETT O. T. (1960) Pre-invasive intraductal cancer. *Surg. Gynecol. Obstet.* **110**, 555–562.

HAAGENSEN C. D. (1971) *Diseases of the Breast*, 2nd ed. Philadelphia, Saunders, pp. 503–520, 586–590.

HUTTER R. V. P. and FOOTE F. W. (1969) Lobular carcinoma in situ. *Cancer* **24**, 1081–1085.

MCDIVITT R. W., HUTTER R. V. P., FOOTE F. W. and STEWART F. W. (1967) In-situ lobular carcinoma—a prospective follow-up study indicating cumulative patient risks. *JAMA* **201**, 82–86.

MCDIVITT R. W., STEWART F. W. and BERG J. W. (1968) *Tumours of the Breast* (*Atlas of Tumour Pathology*, 2nd series, Fascicle 2), 2nd ed. Washington, DC, Armed Forces Institute of Pathology, pp. 22–49.

MUIR R. (1941) Evolution of carcinoma of the breast. *J. Pathol. Bacteriol.* **52**, 155–172.

OZZELLO L. (1971) Ultrastructure of intra-epithelial carcinomas of the breast. *Cancer* **28**, 1508–1515.

SILVERBERG S. G. and CHITALE A. R. (1973) Assessment of significance of proportions of intraductal and infiltrating tumour growth in ductal carcinoma of the breast. *Cancer* **32**, 830–837.

SOMERS S. C. (1969) Histologic changes in incipient carcinoma of the breast. *Cancer* **23**, 822–825.

WHEELER J. E., ENTERLINE H. T., ROSEMAN J. M., TOMASULO J. P., MCILVAINE C. H., FITTS W. T. and KIRSCHENBAUM J. (1974) Lobular carcinoma in situ of the breast. *Cancer* **34**, 554–563.

Br. J. Surg. Vol. 62 (1975) 963–965

The survival rate of men with carcinoma of the breast

ROBERT W. T. SLACK*

SUMMARY

The Cancer Register for the South-West Region of England has been used to examine the survival rate of men with carcinoma of the breast, and a comparison has been made with carcinoma of the breast in women. For all men with carcinoma of the breast the prognosis is worse than for all women, but comparing the prognosis by clinical stage, the difference between men and women is small. However, the survival rate in men under 65 years of age is appreciably better than for men over 65, and for older men the survival rate is considerably less than for women over 65.

CARCINOMA of the breast is rare in men, with an incidence of approximately 1 per cent of the incidence in women. The Registrar General's Statistics for England and Wales for 1972 show that the mortality rate from carcinoma of the breast was 3 per million for men compared with 443 per million for women. Notification of incidence for cancer of the breast occurs at a later age in men than in women; among 507 cases of carcinoma of the breast in men reported from the United States by Moss in 1964 the median age for notification was 64 years compared with 58 years among females. *Fig.* 1 shows a similar shift in age at death from carcinoma of the breast in men compared with women in this country, as recorded by the Registrar General for England and Wales in 1972.

The prognosis for carcinoma of the breast is generally believed to be poorer in men than in women (Vanderbilt and Warren, 1971), and Moss (1964) reported that in his series the 10-year survival rate for women was 49 per cent compared with 32 per cent for men. The discrepancy might be due to the relatively older age of the male patients, but even after correction is made for other causes of death, the female survival rate is 56 per cent compared with 43 per cent in males.

The stage of spread of the disease at the time of notification has an important effect upon survival in both men and women. In Moss's (1964) series in which the stage of the disease was classified as 'localized', 'regional' or 'distant', the prognosis was more favourable for women with localized disease or regional metastases but more favourable for men with distant metastases.

The relationship between the age of notification and the stage of the spread of disease in carcinoma of the male breast is not clear from the studies reported. The present investigation was undertaken to examine the survival rate in carcinoma of the male breast in the South-West Region of England and to find the effects of both age and clinical stage of the spread of the disease upon prognosis.

Patients and methods

The Cancer Register of the South-Western Regional Health Authority was examined and all the records of carcinoma of the male breast notified between 1960 and 1968 were extracted. Patients with carcinoma of the male breast who died from unrelated causes, including one who died from renal complications of carcinomatosis with a primary carcinoma in the kidney, were excluded. Preliminary examination of the whole series showed that no deaths from carcinoma of the male breast occurred more than 7 years after diagnosis; therefore in order to allow a full 7-year follow-up, all the patients presenting in 1968 were excluded. Patients were divided into 10-year age groups and into the four international clinical stage (TNM) groups (Copeland, 1969). Percentage survival rates were calculated by age and stage.

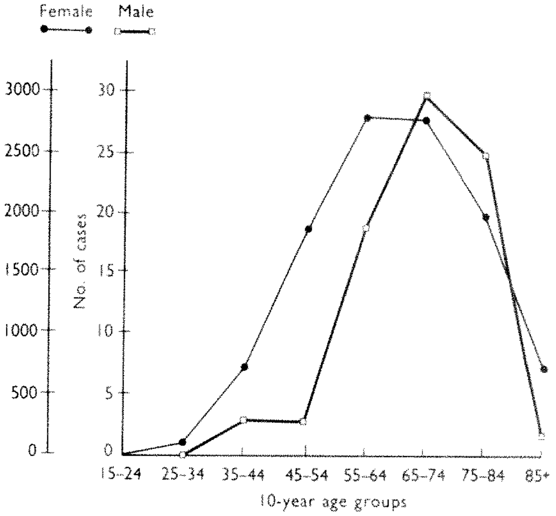


Fig. 1. Number of deaths from carcinoma of the breast in men and women recorded by the Registrar General for England and Wales in 1972.

Results

Between 1960 and 1968, 56 cases of carcinoma of the male breast were reported to the Cancer Registry of the South-Western Regional Health Authority. During that time 6000 cases of carcinoma of the female breast were notified, giving a male to female ratio of 0·93 per cent. After exclusion of 5 patients notified in 1968 and 13 patients who died from causes unrelated to carcinoma of the breast, 38 cases of carcinoma of the male breast were available for study.

---

* Medical student, University of Bristol Medical School, Bristol Royal Infirmary.

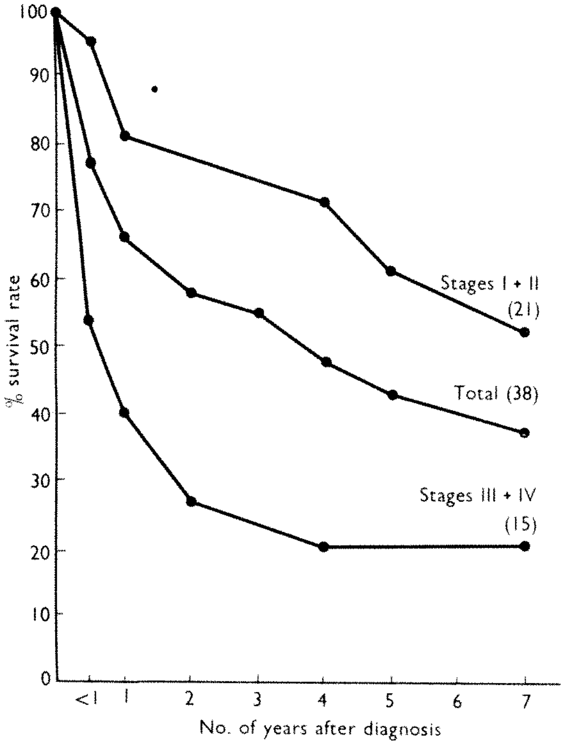


Fig. 2. Percentage survival rate of men with carcinoma of the breast divided by clinical stage of the disease.

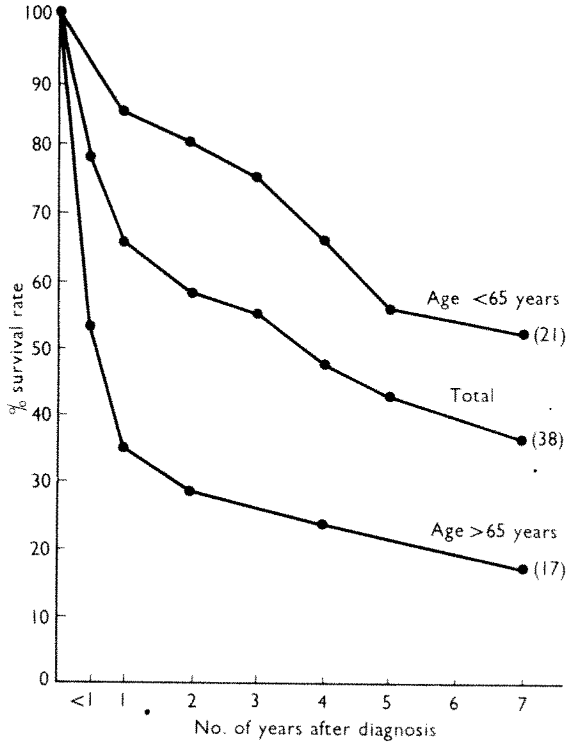


Fig. 3. Percentage survival rate of men with carcinoma of the breast showing those over and under 65 years of age.

Table I: COMPARISON OF AGE OF PATIENTS AND CLINICAL STAGE OF THE DISEASE

	Clinical stage					
Age	I	II	III	IV	Not known	Total
35–44	3	0	0	0	1	4
45–54	1	2	3	0	0	6
55–64	5	2	3	1	0	11
65–74	3	3	2	2	0	10
75+	1	1	3	1	1	7
Total	13	8	11	4	2	38

Table II: PERCENTAGE SURVIVAL RATE ACCORDING TO CLINICAL STAGE OF THE DISEASE

Survival time in years	Clinical stage			
	I	II	III	IV
<1	100·0	87·5	54·5	50·0
1	84·6	75·0	36·4	50·0
2	84·6	75·0	27·3	25·0
3	84·6	75·0	27·3	25·0
4	76·9	62·5	27·3	0·0
5	61·5	62·5	27·3	0·0
6	61·5	62·5	27·3	0·0
7	53·9	50·0	27·3	0·0
Total surviving	53·9	50·0	27·3	0·0

Table III: PERCENTAGE SURVIVAL RATE ACCORDING TO AGE GROUP

Survival time in years	Age group				
	35–44	45–54	55–64	65–74	75+
<1	100·0	100·0	90·9	60·0	42·9
1	75·0	83·3	90·9	60·0	0·0
2	75·0	66·7	90·9	50·0	0·0
3	75·0	66·7	90·9	50·0	0·0
4	50·0	66·7	72·7	40·0	0·0
5	50·0	66·7	54·5	40·0	0·0
6	50·0	66·7	54·5	40·0	0·0
7	50·0	50·0	54·5	30·0	0·0
Total surviving	50·0	50·0	54·5	30·0	0·0

Table I shows the numbers of patients according to age and clinical stage at the time of presentation of the disease.

Table II shows the percentage survival rate of the 36 patients in whom the stage of the disease was notified. In 2 patients the stage of the disease was unknown. *Fig.* 2 shows the percentage survival rate of the total group and of two subgroups, dividing the patients into Stages I and II and Stages III and IV for comparison.

Table III shows the percentage survival rate of the 38 patients divided into 10-year age groups. *Fig.* 3 shows the percentage survival rate in the whole group and in two age subgroups—those above and below 65 years.

Discussion

It has been thought that men with carcinoma of the breast have a worse prognosis than women, and this view was upheld by Somerville (1951), who considered that the unfavourable prognosis in men was due to the late presentation of the patients. Comparing the survival rate of men in the present series with that of women with carcinoma of the breast reported by Haagensen (1971), the 7-year survival rate of the total group of men of 37 per cent is indeed worse than the 10-year survival rate for women of 63 per cent. Unfortunately, in Haagensen's series the stage of the disease was determined by the Columbia Clinical Classification (Haagensen et al., 1963) into Stages A, B, C and D, and so the stages of disease in Haagensen's series are not strictly comparable with the international TNM staging used by the South-Western Regional Cancer Registry, but there is a close relationship between them (Handley, 1967). When the survival rate by stage is compared in men and women, only a small difference is found. Combining Stages I and II in men, the 7-year survival rate is 52·4 per cent, while in women, combining Stages A and B, the 10-year survival rate is 68 per cent. There is much less difference in survival rate for men and women presenting at the later stages of the disease. For Stages III and IV combined, the 7-year survival rate in men is 20 per cent, compared with a 10-year survival rate in women presenting with Stages C and D of 24 per cent. Thus, the overall poorer prognosis in men seems to be due to an excess of men presenting at a late clinical stage of the disease, as suggested by Somerville (1951).

When a comparison of survival rates of men and women with carcinoma of the breast is made by age a marked difference is found. For men under the age of 65 the 7-year survival rate is 52 per cent compared with a 10-year survival rate in women under 65 of 64 per cent. For men over 65 the 7-year survival rate is 18 per cent compared with a 10-year survival rate in Haagensen's (1971) series of 51 women over 65 years of 57 per cent. If there was evidence that a higher proportion of men over 65 presented with carcinoma of the breast at Stages III and IV than at Stages I and II, the explanation of the poor prognosis in older men might be found in the advanced stage of the disease. However, in the present series nearly equal numbers of patients with Stages III and IV were over and under 65, compared with 17 over 65 and 21 under 65 in the whole series (*see Table I*).

There seems little doubt that the prognosis for men over 65 with carcinoma of the breast is worse than the prognosis for younger men and that this difference is not explained by the later stage of the disease at presentation. An explanation of the poor prognosis in older men may lie in the decline of male hormones with age.

Acknowledgements

I am very grateful to Mr R. E. Horton for his encouragement of this investigation and for his helpful criticisms of the manuscript.

References

COPELAND M. D. (1969) T.N.M. Staging. American Joint Committee on Cancer Staging and End Results Reporting Objectives and Progress. *Cancer* **18**, 1637–1740.

HAAGENSEN C. D. (1971) *Diseases of the Breast*, 2nd ed. Philadelphia, Saunders, p. 658.

HAAGENSEN C. D., COOLEY E., KENNEDY C. S. MILLER E., HANELLEY R. S., THACKRAY A. C., BUTCHER H. R., DAHL-IVERSEN E., TOBIASSEN T., WILLIAMS I. G., CURWEN M. P., KAAE S. and JOHANSEN H. (1963) Treatment of early mammary carcinoma. A cooperative international study. *Ann. Surg.* **157**, 157–161.

HANDLEY R. S. (1967) Indications and contraindications for mastectomy. *JAMA* **200**, 610–611.

MOSS N. H. (1964) Cancer of the male breast. *Ann. N Y Acad. Sci.* **114**, 937–950.

REGISTRAR-GENERAL (1972) *Statistical Review of England and Wales*, Part I, tables: medical. London, HMSO.

SOMERVILLE P. (1951) Carcinoma of the male breast. *Br. J. Surg.* **39**, 296–303.

VANDERBILT P. C. and WARREN S. E. (1971) Forty year experience with carcinoma of the male breast. *Surg. Gynecol. Obstet.* **133**, 629–633.

Br. J. Surg. Vol. 62 (1975) 966–972

Operative cholangiography: a reappraisal based on a review of 400 cholangiograms

IRWIN FARIS, JAMES P. S. THOMSON, D. J. GRUNDY
AND L. P. LE QUESNE*

SUMMARY

In the period 1957–72, 426 patients were operated upon for calculous disease of the biliary tract. For various reasons pre-exploratory operative cholangiography was not performed in 26 patients, but in the remaining 400 patients this examination was the major determinant as to whether or not the common duct contained calculi, and hence required exploration. Analysis of this series of 400 patients shows that without operative cholangiography (a) ductal stones would have been overlooked in 16 of the 78 patients with stones in the common duct (4 per cent of the whole series; 20·5 per cent of those with stones in the common bile duct); (b) exploration of the common duct would have been required in a further 48 (15 per cent) of the 322 patients without stones in the common duct, giving a positive yield from operative cholangiography in 64 patients (16 per cent) in the whole series. Negative exploration of the common duct was performed in only 31 patients, that is 29 per cent of the patients whose duct was explored but only 7·8 per cent of the whole group.

The criteria by which an operative cholangiogram should be assessed were re-evaluated in the light of the findings in these 400 patients. In general the criteria of normality previously described were affirmed, and the following points established:

a. In the absence of a filling defect the diameter of the duct is the most important indication of the presence of a stone.

b. There is a statistically significant increase in the diameter of the common duct with age, and though not great this could, if neglected, give rise to error in the interpretation of the cholangiogram in younger patients.

c. Even within the overall normal range of duct diameter (<12 mm) the wider the duct, the greater is the chance of it harbouring a stone.

d. Impaired flow of contrast material into the duodenum is significantly related to duct diameter.

e. Impaired flow of contrast material into the duodenum and failure to delineate the terminal segment of the duct tend to occur together; they may occur in a duct free of stones and if they are the only abnormality the examination should be repeated after the inhalation of amyl nitrite.

This study confirms that operative cholangiography is the most accurate method at present available of determining whether or not the common duct contains a stone (or stones), and hence requires exploration.

OPERATIVE cholangiography is now a well-established technique. Many authors have shown that it detects stones in the common bile duct which would otherwise have been overlooked and reduces the number of unnecessary explorations (Schulenburg, 1969; Lawson and Gunn, 1970; Havard, 1970; McEvedy, 1970; Kakos et al., 1972). Despite this there is still opposition to its routine use.

This paper reviews our experience with this technique and allows a reappraisal of the features of a normal cholangiogram. The value of operative cholangiography in the diagnosis of stone in the common duct is compared with conventional clinical and operative indications.

Description of series

During the years 1957–72, 426 operations for gallstones were carried out in the clinical service of the senior author. There were 332 patients with stones in the gallbladder (GB) only and 94 patients with stones in the common bile duct (CBD); of the latter group, 12 patients had undergone a previous biliary tract operation. For a variety of reasons operative cholangiograms were not performed in 26 patients, leaving for analysis 400 patients with operative cholangiograms (GB group 322; CBD group 78). These patients were operated upon by a number of surgeons, many of whom were registrars in training.

The distribution of the age of the patients is shown in *Fig.* 1. The CBD group are significantly older than the GB group ($t = 5{\cdot}876$, $P < 0{\cdot}001$). There is no difference in the sex distribution between the two groups.

Pain was a symptom in 304 (94·6 per cent) patients of the GB group. In 7 patients cholecystectomy was performed concurrently with another procedure, and in 11 patients symptomless gallstones were removed at elective operation. There were 2 deaths following operation.

Methods

Operative cholangiography was performed through a catheter introduced into the cystic duct by the technique described by Le Quesne (1960). In patients with an apparently normal duct radiographs were taken following the slow injection of successively 2, 3 and 5 ml of 25 per cent sodium diatrizoate BP (Hypaque), but in those with an obviously dilated CBD the amount injected before the second and third exposures was increased. The CBD was judged to be

---

* Department of Surgical Studies, The Middlesex Hospital Medical School, London.
Requests for reprints to L. P. Le Quesne.

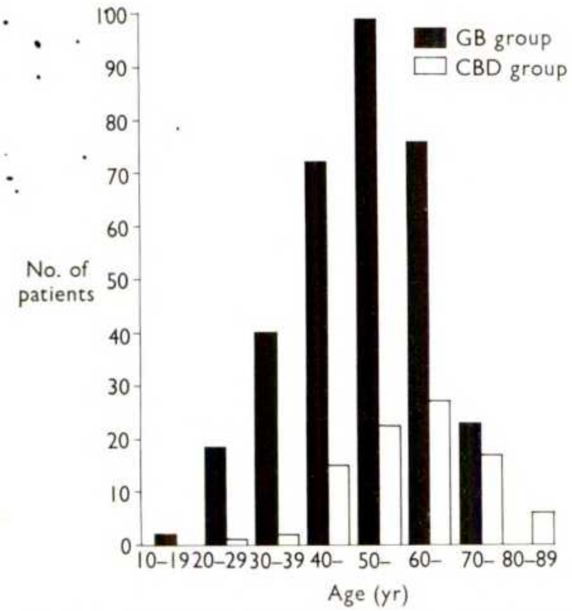


Fig. 1. Age distribution of the whole series (i.e. 426 patients). The age of patients with stone in the CBD is significantly greater than in those without ($t = 5{\cdot}876$, $P < 0{\cdot}001$).

normal if the cholangiogram fulfilled the following criteria (Le Quesne, 1960):

1. The diameter of the CBD as measured on the radiograph did not exceed 12 mm.
2. There were no defects within the CBD.
3. The narrow segment at the lower end of the CBD was clearly seen on at least one film.
4. There was flow of contrast medium into the duodenum on the first film; provided that the examination was in all other respects normal, flow seen initially on the second film was accepted as normal.

Fig. 2 shows an example of a normal operative cholangiogram fulfilling these criteria.

At the time of the patient's discharge from hospital the relevant clinical and radiological information was entered on a card. These cards provided the data for this survey.

In the analysis that follows the clinical and operative criteria for exploration of the CBD are defined as:

1. Jaundice, present or in the recent past.
2. Operative finding of a dilated CBD or palpable stones within the CBD.
3. The presence of multiple stones (three or more) within the gallbladder.
4. Demonstration of a defect in the CBD on a preoperative intravenous cholangiogram. This investigation was performed on 130 patients in the GB group and on 57 patients in the CBD group.

The frequency of occurrence of these criteria is shown in *Tables I* and *II*.

Results

The following analysis is based on the 400 patients upon whom an operative cholangiogram was performed.

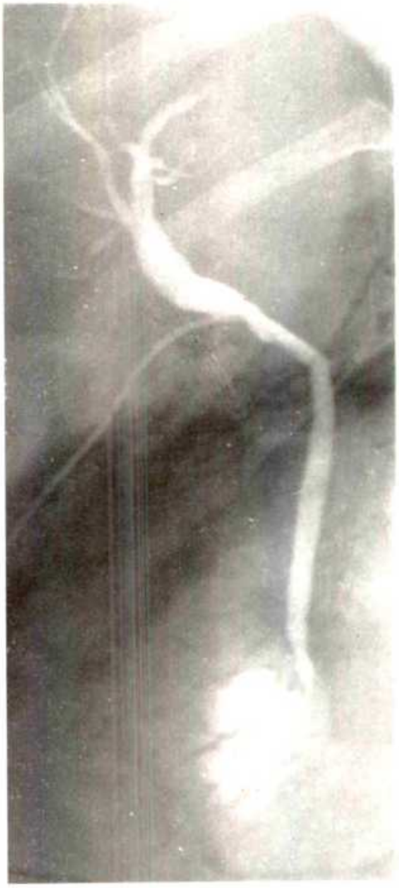


Fig. 2. First film from a normal operative cholangiogram. Note the free flow of contrast material into the duodenum, the visualization of the whole of the narrow segment and the absence of filling defects. This picture is slightly enlarged from the original radiograph, in which the diameter of the common duct was 9 mm.

Table I: FREQUENCY OF CONVENTIONAL CRITERIA FOR EXPLORATION OF THE CBD

Criteria	GB group No.	GB group %	CBD group No.	CBD group %
Jaundice, present or recent past	46	14	49	63
Dilated duct at operation	15	5	54	69
Stone palpable at operation	2*		50	64
Multiple stones palpable in gallbladder (3 or more)	173	55	34	44

* These calculi were found to be impacted at the lower end of the cystic duct.

Table II: INCIDENCE OF A DEFECT SHOWN IN THE CBD ON INTRAVENOUS CHOLANGIOGRAPHY

Intravenous cholangiogram	GB group No.	GB group %	CBD group No.	CBD group %
Number performed	130	40	57	73
Number showing defects in CBD	1		33*	

* Thus, this preoperative investigation only indicated the presence of calculi in the CBD in 58 per cent of the patients.

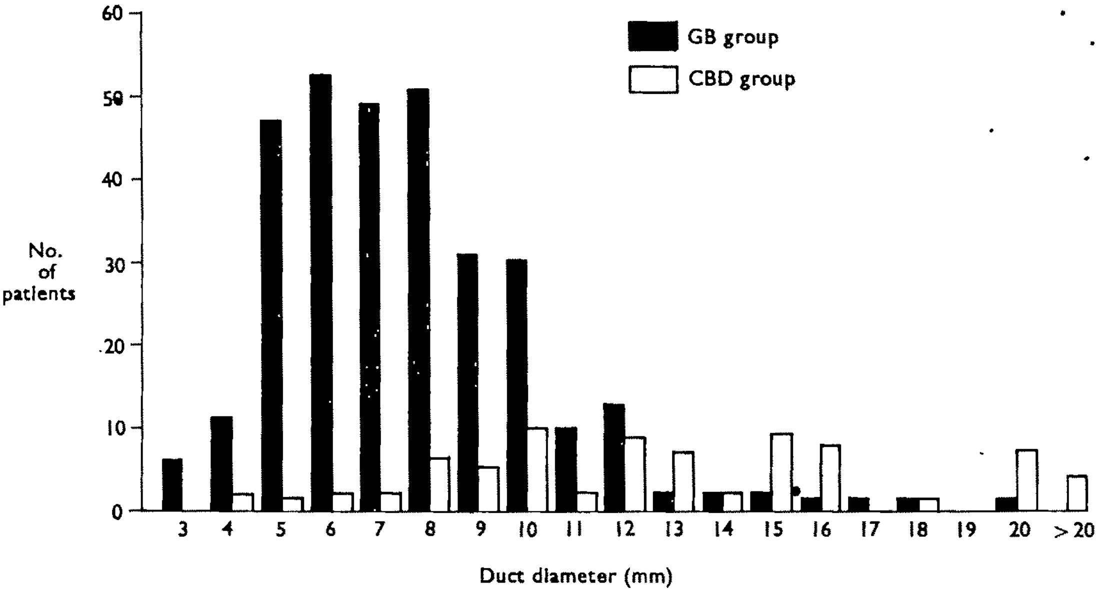


Fig. 3. Distribution of the duct diameter in the 400 patients who had operative cholangiography. The diameter of the duct in the CBD group was significantly larger than the GB group ($t = 10{\cdot}09$, $P<0{\cdot}001$).

Table III: OVERALL VALUE OF OPERATIVE CHOLANGIOGRAPHY

	GB group			CBD group		
		Cholangiogram			Cholangiogram	
	Total	Normal	Abnormal	Total	Normal	Abnormal
No clinical or operative indications for exploration of CBD	249	243	6*	16	0	16
Clinical and/or operative indications for exploration of CBD	73	53†	20*	62	0	62

* Negative exploration of CBD. † CBD explored in 5 cases.

Assessment of overall value of cholangiography

The overall value of the routine performance of this investigation can be gauged from *Table III*. In 16 patients (4 per cent) the cholangiogram revealed the presence of an unsuspected stone in the duct. In 53 patients in whom there were clinical and/or operative indications of a stone in the duct, the cholangiogram revealed a normal duct. In 5 of these 53 patients, despite the normal cholangiogram, the common duct was explored, because of a recent history of jaundice in 4, and the finding on prior intravenous cholangiography of an apparently dilated common duct in the fifth. Thus, in 64 patients [16+(53−5)] (16 per cent) the operative cholangiogram gave positively useful information, resulting in the correct decision being made as to whether or not the duct should be explored, and in a further 5 patients (making 17 per cent in all) it gave the correct information which was not acted upon for the reasons stated above.

In 26 patients the cholangiogram was interpreted as indicating the presence of a stone, but a stone was not found on exploration of the duct (i.e. false positives 6·5 per cent). Of these 26 patients, 9 had what was thought to be a filling defect. The remaining 17 patients had abnormalities of one or more of the other criteria, commonly a failure in flow. Of these 17, 13 had in addition clinical and/or operative indications for exploration of the duct.

In the whole group the CBD was explored in 109 patients (27·3 per cent), and in 78 (71·5 per cent) of these, stones were found in the CBD.

Analysis of cholangiograms

Duct diameter: The distribution of the diameter of the duct is shown in *Fig*. 3. Common bile ducts which contained stones were significantly larger than those which were stone-free ($t = 10{\cdot}09$, $P<0{\cdot}001$).

In the GB group (i.e. patients with a normal CBD) there was a significant correlation between duct diameter and age ($r = 0{\cdot}27$, $P<0{\cdot}001$). This is shown in *Fig*. 4 on which the 95 per cent tolerance limits are shown in addition to the regression line. The age and duct diameter of patients in the CBD group are plotted in relation to these boundaries in *Fig*. 5. Whilst 46 patients (59 per cent) with stones in the CBD had a dilated duct, it is to be noted that 32 (41 per cent) of the patients with stones in the CBD have duct diameters within the 95 per cent tolerance limits for stone-free ducts. Analysis of these figures in greater detail (*Fig*. 6) shows the percentage chance of having a stone in the CBD for a duct of given diameter. This relationship between duct diameter and the chances of the duct containing a stone is highly significant ($r = 0{\cdot}9698$, $P<0{\cdot}001$) and is unaffected by correction for age. It can be seen, for example, that a duct at the upper limit

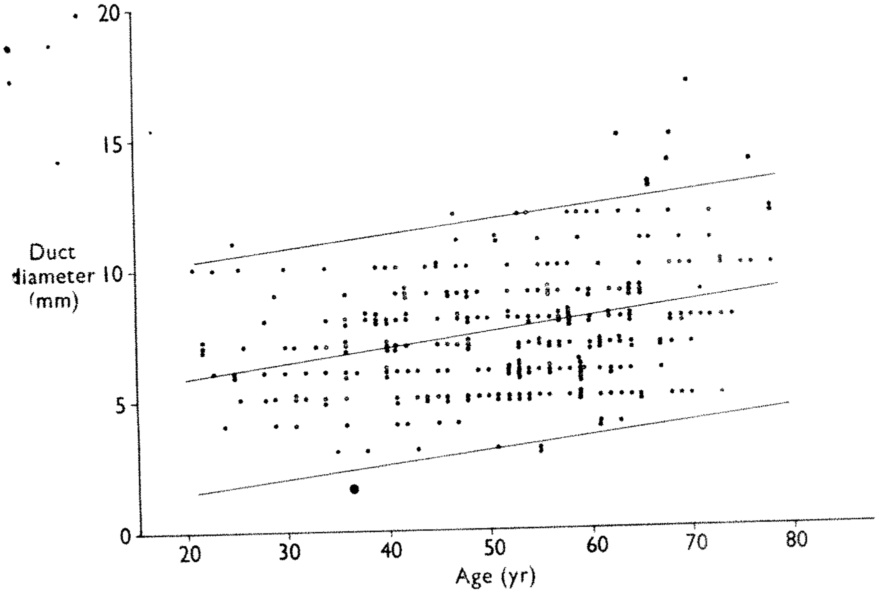


Fig. 4. Regression line and 95 per cent tolerance limits for the correlation between age and duct diameter for the GB group ($r = 0{\cdot}27$, $n = 307$, $P < 0{\cdot}001$). The diameter of the duct was not recorded in 15 patients of this group.

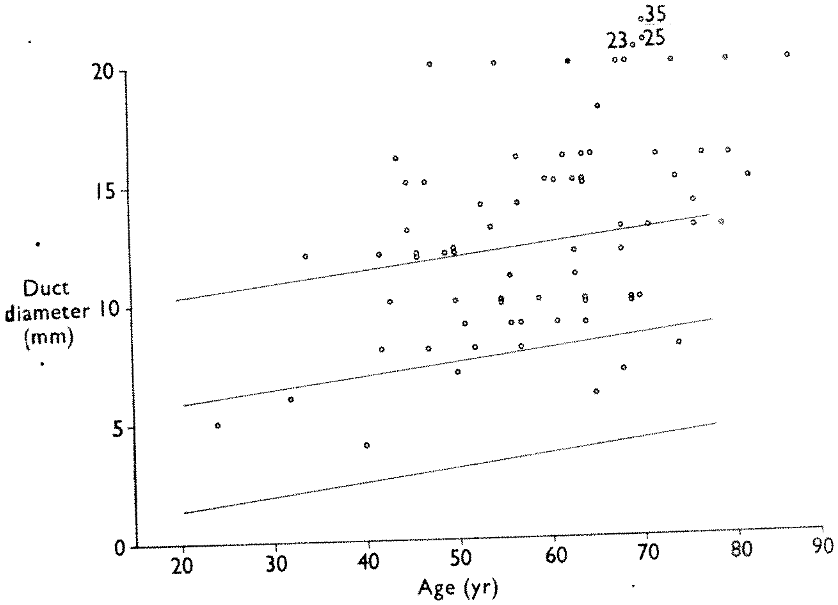


Fig. 5. Each point represents the age and duct diameter of the 78 patients in the CBD group. These have been plotted in relationship to the regression line and 95 per cent tolerance limits derived in *Fig.* 4.

of the normal range (11–12 mm) has a 32 per cent chance of containing a stone.

Filling defects: Filling defects were demonstrated in 67 (86 per cent) of the patients with stones in the CBD. However, in 11 patients (14 per cent) with a stone in the duct a defect was not seen and the correct diagnosis made from the other criteria described. As previously mentioned, in 9 patients in the GB group a filling defect was seen on the cholangiogram but no stone was found on exploration of the duct; review of these films suggests that in each instance the defect was caused by an air bubble.

Demonstration of the narrow segment: The narrow segment was seen less frequently in patients with stones in the CBD than in those without (*Table IV*) ($\chi^2 = 107$, $P \leqslant 0{\cdot}001$). The segment was not seen in 7 per cent of the GB group and in 55 per cent of the CBD group.

Flow into the duodenum: *Table V* indicates the radiograph on which flow into the duodenum was first seen.

There was a distinct difference between the two groups in the time of appearance of contrast medium in the duodenum. Further analysis showed that there was also a highly significant relationship between duct diameter and delay in flow into the duodenum ($r = 0{\cdot}5426$, $n = 377$, $P \leqslant 0{\cdot}001$), a large duct being associated with delayed flow into the duodenum.

Use of amyl nitrite: A common cause of a false positive cholangiogram (i.e. one apparently indicating the presence of a stone in the CBD) is a failure to demonstrate the narrow segment and delayed flow of contrast into the duodenum. Insufflation of amyl nitrite into the airway followed by repetition of the cholangiogram can resolve some of these difficulties (Le Quesne, 1960). This technique was used in 13 patients in whom the CBD was of normal calibre and no defects were seen but in whom there was no flow of contrast into the duodenum and no demonstration of the narrow

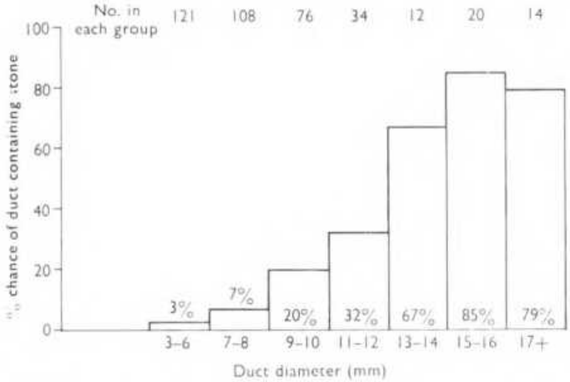


Fig. 6. Percentage chance of a duct of given diameter containing a stone.

Table IV: DEMONSTRATION OF THE NARROW SEGMENT

	GB group		CBD group	
	No.	%	No.	%
Narrow segment seen	291	90	33	42
Narrow segment not seen	22	7	43	55
Information not available	9	3	2	3

Table V: DEMONSTRATION OF FLOW OF CONTRAST INTO THE DUODENUM

	GB group		CBD group	
	No.	%	No.	%
Radiograph on which flow first seen				
1	229	71	14	18
2	39	12	23	29
3	13	4	10	13
No flow seen	18	6	31	40
Information not available	23	7	Nil	

Eleven of the 18 patients in the GB group in whom no flow was seen had a repeat examination after amyl nitrite (*see* text revealing a duct in all respects normal. Note that in approximately 80 per cent of the GB group flow was first seen in the first or second film.

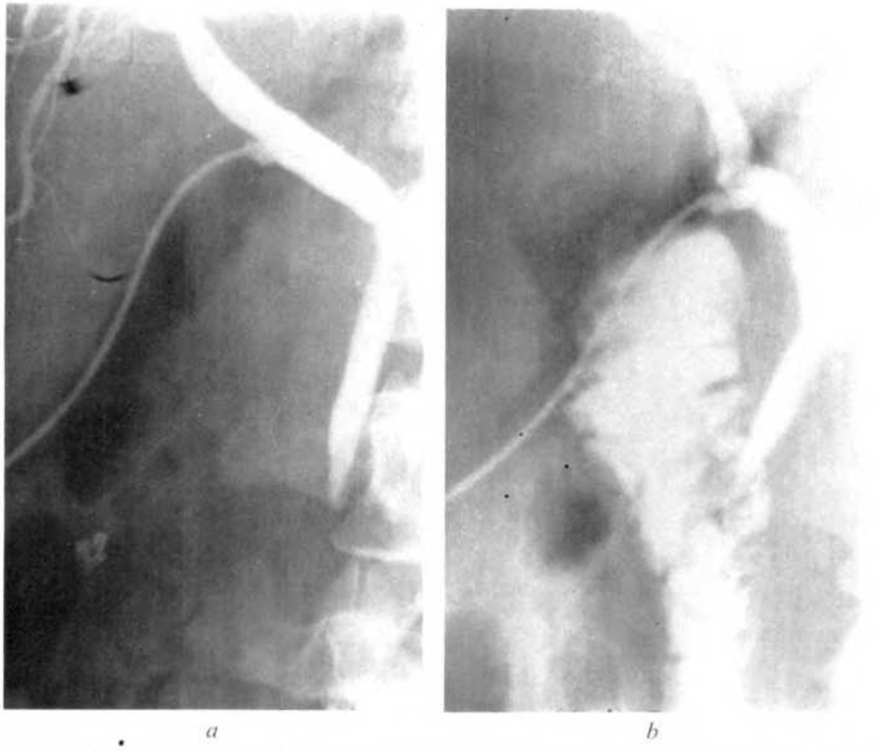


Fig. 7. *a*, One of the three cholangiograms from a series in which the only abnormality was absence of flow, with failure to demonstrate the narrow segment. *b*, Repetition of the examination after the inhalation of amyl nitrite showed free flow of the contrast material and a cholangiogram in all respects normal.

segment. In 11 of these patients the second cholangiogram was normal (*Fig.* 7) and accordingly an exploration was not performed; in 2 patients stones were demonstrated in the CBD.

Discussion

Overall value

This series differs from several other published reports of this technique in that the operations were performed by a number of surgeons including registrars of varying experience. This is important as it is at least possible that the good results obtained in many personal series depend on the interest of the observer, and may not be reproduced when the technique is adopted by others.

The major aim of operative cholangiography is to add precision to the diagnosis of stone in the CBD. This should result in: the detection of stones in the CBD which would otherwise have been overlooked; a reduction in the number of normal ducts explored.

In 16 (20·5 per cent) patients with stones in the CBD there were neither clinical nor operative indications for choledochotomy, the diagnosis being made solely on the basis of an abnormal cholangiogram. The negative exploration rate is commonly expressed as a percentage of the number of duct explorations performed. In this series the rate was 29 per cent. This compares with a negative exploration rate reported by other authors using cholangiography of 28–44 per cent (Wheeler et al., 1970; Kakos et al., 1972; Way et al., 1972; Glenn, 1974), and 46–58 per cent without cholangiography (Schofield and Macleod, 1966; Wheeler et al., 1970). We were unable to demonstrate a fall in the negative exploration rate with time, probably because of the number of surgeons who performed the operations in this series.

The biggest single cause of a false positive cholangiogram is the presence of air bubbles; these can be avoided by scrupulous attention to technical details, and the greatest care must be taken to avoid their introduction into the duct. The most severe difficulties in interpretation occur when with a duct of normal diameter, in the absence of filling defects, there is no flow of contrast into the duodenum and there is no demonstration of the narrow segment. These appearances are due to contraction of the muscle surrounding the lower end of the duct. This may be caused by a small stone in the duct, but is more commonly due to other factors such as the variety of pharmacological agents used in anaesthesia. From the evidence of this study it is clear that repetition of the examination after the inhalation of amyl nitrite is a valuable method of clarifying the situation. In fact this technique was rarely, if ever, used by registrars, and if it had been it would probably have resulted in avoidance of exploration of a number of ducts which were in fact explored solely because of abnormalities of flow or failure to demonstrate the terminal narrow segment. If there is still doubt after the second examination it need hardly be said that the common duct must be explored.

Forty-eight of the 135 patients (36 per cent) who had clinical or operative indications for exploration of the CBD were saved this unnecessary procedure by the demonstration of a normal operative cholangiogram. It is arguable that in some of these patients a stone in the duct was in fact missed. However, close follow-up of patients early in this series (Chapman et al., 1964) and the reports of other authors (Ferguson and Estes, 1967; Glenn, 1974) indicate that this is most unlikely, and that an operative cholangiogram fulfilling the criteria set out earlier can be relied upon with confidence as evidence of a normal stone-free duct. In view of this it is now our practice not to explore the duct of patients with a history of jaundice, even if recent, if the operative cholangiogram is in all respects normal.

The normal cholangiogram

This study has allowed us to reassess our criteria of the normal cholangiogram. The increase in duct size with age has long been suggested but not clearly defined. We have demonstrated a significant increase in duct diameter with age. This may be important in a young patient in whom a 10- or 11-mm diameter CBD may be abnormally dilated. However, the duct diameter is not an absolute indicator of the presence of a stone in the CBD, since, from *Figs.* 4 and 5, it can be seen that two-fifths of the patients with CBD stones have ducts of normal calibre. In addition, *Fig.* 6 shows that there is no upper limit of duct diameter above which the incidence of stones suddenly increases.

The analysis confirms the validity of current criteria of the flow of contrast medium into the duodenum and the demonstration of the terminal narrow segment of the common bile duct. There is no difference in the discrimination obtained if these criteria are considered separately or in combination. The demonstration that delay in flow of contrast into the duodenum is directly proportional to the duct diameter may indicate inadequate filling, or it may be due to obstruction which results in failure of flow and dilatation of the duct. In this regard an injection of contrast medium at standard pressure (Daniel, 1972), rather than of standard volume, might distinguish between these causes and represent an improvement in technique.

Evaluation of conventional indications

The results of this study emphasize the inadequacy of conventional indications in the diagnosis of stone in the CBD. Analysing the whole group of 400 patients it was found that a patient who gives a history of jaundice is as likely to have stones in the gallbladder only as he is to have a stone in the common bile duct (*Table I*). Way et al. (1972) found jaundice more commonly associated with stones in the CBD, but when jaundice was the only indication for exploration stones were found in the CBD in only 6 of their 17 patients.

It is frequently recommended that the CBD should be explored in all patients with multiple stones in the gallbladder. The evidence from this study does not support this assertion. (In this analysis 'multiple stones' means more than 3, and if the phrase 'a few stones' was used the patient was considered not to have multiple stones.) As will be seen from *Table I* there was no significant difference in the incidence of multiple stones in the two groups, a finding in conformity with that of Mullen et al. (1972).

Intravenous cholangiography may be useful in demonstrating a stone in the CBD. In the 57 patients in the CBD group in whom this examination was performed a stone was demonstrated in 33, but in 24 patients the preoperative examination was considered normal. This confirms the finding of Grundy et al. (1972) that an operative cholangiogram is more accurate than intravenous cholangiography in the diagnosis of stone in the common duct.

This study also reaffirms that operative assessment (by inspection and palpation) of the CBD is not a sufficiently sensitive method of detecting stones. In this series only two-thirds of the stones in the CBD were palpable. It was anticipated that increasing reliance on the operative cholangiogram would result in less careful palpation of the duct, but the number of stones felt in this series (64 per cent) is similar to that in Daniel's (1972) series where the primary method of diagnosis was careful palpation. Determination of the duct size at operation may be difficult and it should be remembered that two-fifths of ducts containing stones were of normal calibre.

Conclusion

This study of 400 patients undergoing cholecystectomy with operative cholangiography confirms that this method of examination is the most reliable investigation available for determining whether or not the duct contains a stone or stones. Further, the study reaffirms the criteria of normality previously described, and shows that the greater the diameter of the duct as seen on cholangiography, the greater the chance of it harbouring a stone, whether or not the duct diameter is within normal limits.

Acknowledgements

Our thanks are due to the staff of the Department of Radiodiagnosis, The Middlesex Hospital, for their collaboration throughout the years of this study and the Department of Medical Illustration for their help with the illustrations.

References

CHAPMAN M., CURRIE R. C. and LE QUESNE L. P. (1964). Operative cholangiography—an assessment of its reliability in the diagnosis of a normal, stone-free common bile-duct. *Br. J. Surg.* **51**, 600–601.

DANIEL O. (1972) The value of radiomanometry in bile duct surgery. *Ann. R. Coll. Surg. Engl.* **51**, 357–372.

FERGUSON W. H. and ESTES J. T. (1967) Value of routine operative cholangiograms. *Am. J. Gastroenterol.* **48**, 311–318.

GLENN F. (1974) Retained calculi within the biliary ductal system. *Ann. Surg.* **179**, 528–537.

GRUNDY D. J., KING P. A. and LLOYD G. (1972) Comparative evaluation of preoperative and operative radiology in biliary-tract disease. *Br. J. Surg.* **59**, 205–208.

HAVARD C. (1970) Operative cholangiography. *Br. J. Surg.* **57**, 797–807.

KAKOS G. S., TOMPKINS R. K., TURNIPSEED W. and ZOLLINGER R. M. (1972) Operative cholangiography during routine cholecystectomy—a review of 3,012 cases. *Arch. Surg.* **104**, 484–487.

LAWSON R. A. M. and GUNN A. A. (1970) The value of operative cholangiography. *J. R. Coll. Surg. Edin.* **15**, 222–227.

LE QUESNE L. P. (1960) Cholangiography. *Proc. R. Soc. Med.* **53**, 852–855.

MCEVEDY B. V. (1970) Routine operative cholangiography. *Br. J. Surg.* **57**, 277–279.

MULLEN J. L., ROSATO E. F., IPSEN J. and ROSATO F. E. (1972) Gallstone characteristics in the diagnosis of choledocholithiasis. *Ann. Surg.* **176**, 718–720.

SCHOFIELD G. E. and MACLEOD R. G. (1966) Sequelae of cholecystectomy. *Br. J. Surg.* **53**, 1042–1045.

SCHULENBURG C. A. R. (1969) Operative cholangiography: 1,000 cases. *Surgery* **65**, 723–739.

WAY L. W., ADMIRAND W. H. and DUNPHY J. E. (1972) Management of choledocholithiasis. *Ann. Surg.* **176**, 347–357.

WHEELER M. H., RAKSASOOK S. and WILLIAMS J. A. (1970) Operative cholangiography. Its effect on the practice of cholecystectomy. *Br. Med. J.* **4**, 161–164.

Br. J. Surg. Vol. 62 (1975) 973–976

Carcinoma of the duodenum: its preoperative diagnosis

K. SATAKE, M. SOWA, K. YAMASHITA, K. KAMINO,
H. KINOSHITA, M. KATO AND K. UMEYAMA

SUMMARY

Carcinoma of the duodenum, although uncommon, can be diagnosed by direct visualization, photography of the tumour and biopsy by the fibre-duodenoscope. The duodenoscopic examination may not only distinguish carcinoma of the duodenum from pancreatic carcinoma, ampullary carcinoma and secondary tumour from an adjacent organ but will also enable a correct diagnosis to be made early in the course of the disease.

It is therefore suggested that duodenoscopy and biopsy will increase the resectability and 5-year survival rate.

CARCINOMA of the duodenum is an uncommon disease and most of our knowledge is based on necropsy studies (Eger, 1933; Willis, 1948). In the past decade only a small number of individual cases with satisfactory results following treatment have been reported (Warren et al., 1962; Cartese and Cornall, 1972).

Early diagnosis of this disease is extremely difficult. However, the development of the fibre-duodenoscope for duodenal observation has opened a new diagnostic field and made possible early detection and accurate diagnosis of this disease before operation.

In this paper 2 new cases are presented and discussed together with cases reported in the literature, particular attention being paid to those with an accurate preoperative diagnosis. The 2 cases reported here were diagnosed as duodenal tumour by upper gastro-intestinal examination, and the diagnosis was confirmed by duodenoscopy and biopsy.

Case reports

Case 1: A 64-year-old man complained for a month of malaise, weight loss and dull back pain. He had vomited three or four times a day for weeks but gave no history of dysphagia, haematemesis, melaena or jaundice. About a year previously he had undergone gastrectomy (Billroth I) for gastric ulcer at another hospital. Subsequently he had been quite well and free of symptoms until the present episode.

On admission to Osaka City University Hospital the patient was thin, appeared pale and chronically ill but no jaundice was noted. Abdominal examination was essentially normal except for the upper median gastrectomy incision, and rectal examination was normal.

Laboratory investigations on admission revealed a haemoglobin of 8·0 g/100 ml with a red blood cell count of 3 160 000/mm³. Serum electrolyte levels were within normal limits as were the serum glutamic oxalo-acetic transaminase, serum bilirubin and alkaline phosphatase values. The total serum protein value was 6·0 g/100 ml and albumin 3·6 g/100 ml. Stool samples were strongly positive for occult blood. Examination of the upper gastro-intestinal series showed a 2 × 3 cm filling defect of the distal duodenum with slight dilatation proximally (*Fig.* 1). Duodenoscopic examination revealed normal stomach and proximal duodenum, but a well-localized 2 × 3-cm tumour with ulceration in its centre was found in the third part of the duodenum. Biopsy of the tumour showed a well-differentiated adenocarcinoma.

An extended pancreatoduodenectomy was performed with removal of the anastomotic region of the stomach, the duodenum, head and body of the pancreas and regional lymph-nodes. No distant lymph node swelling was found. Reconstruction was accomplished by suturing the common bile duct to the proximal end of the jejunum, implanting the pancreatic duct by direct suture of the pancreas and jejunum in an end-to-side fashion and constructing a gastrojejunostomy.

The pathologist reported that section of the tumour showed a well-differentiated adenocarcinoma with extension through the mucosa to the muscle layer but not to the serosa (*Figs.* 2, 3). Section of regional lymph nodes showed no involvement.

Fourteen months after discharge there was no evidence of recurrence and the patient was well and working.

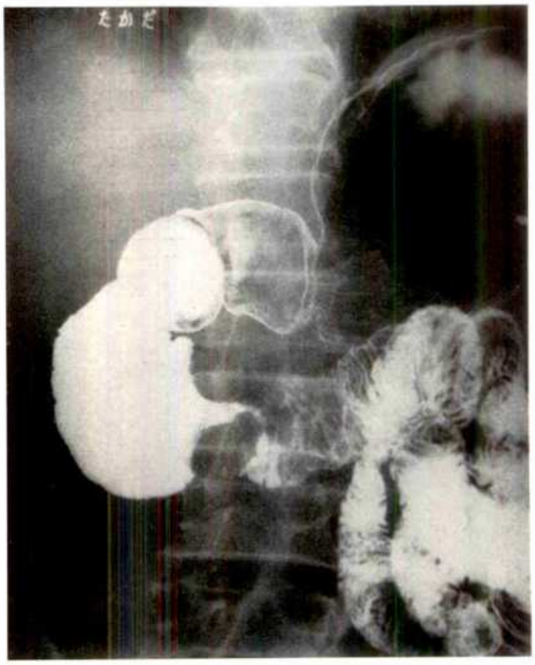


Fig. 1. *Case* 1. Upper gastro-intestinal film showing a 2 × 3-cm filling defect in the third part of the duodenum with slight dilatation proximally.

Case 2: A 35-year-old man, complained of crampy epigastric pain for 7 months. A month prior to his admission his symptoms had increased in severity, with progressive and continuous pain which radiated to his back. He had been treated for about 6 months at another hospital following diagnosis of duodenal ulcer but had shown no improvement.

On admission to Biwako Hospital he was thin and chronically ill. He stated that over the past 2 months he had lost about 7 kg in weight. Abdominal examination revealed tenderness

---

* First Department of Surgery, Osaka City University Medical School, and Department of Surgery, Biwako Hospital, Osaka, Japan.

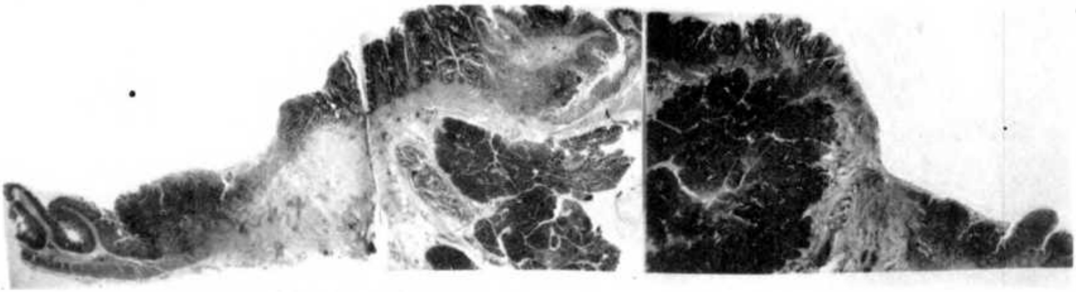


Fig. 2. *Case* 1. Cross-section of the duodenal tumour.

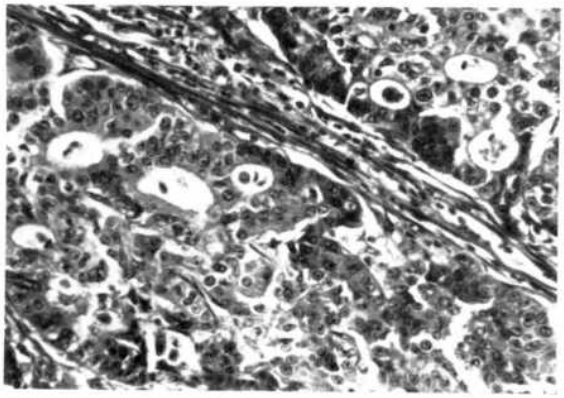


Fig. 3. *Case* 1. Photomicrograph showing a well-differentiated adenocarcinoma. (× 24.)

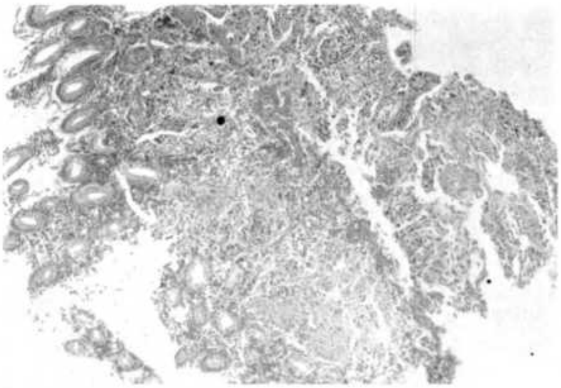


Fig. 5. *Case* 2. Biopsy of the tumour showing an adenocarcinoma of the duodenum. (× 60.)

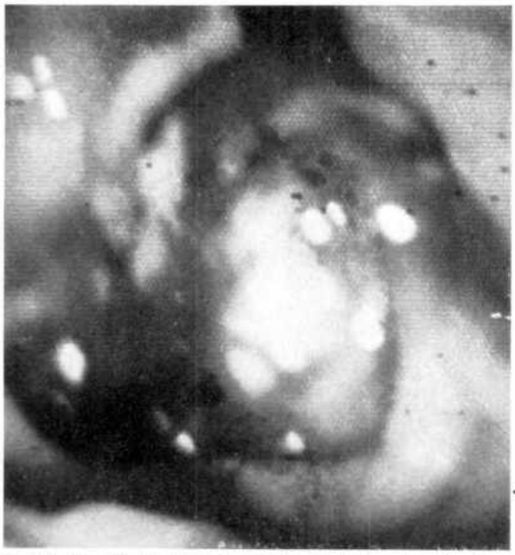


Fig. 4. *Case* 2. Endoscopic photograph showing the tumour and ulceration in the duodenum.

in the epigastrium with muscle rigidity, and a 4 × 5-cm tumour-like resistance was palpable in the epigastrium. Rectal examination was normal.

Laboratory investigations on admission revealed a haemoglobin level of 11·0 g/100 ml with a red blood cell count of 3 290 000/mm^3. Serum electrolyte levels were within normal limits. The serum glutamic oxalo-acetic transaminase was 110 Karmen units and the alkaline phosphatase was also slightly elevated, but the serum bilirubin was within normal limits. The total serum protein value was 6·6 g/100 ml and albumin 3·9 g/100 ml. Stool samples were strongly positive for occult blood.

Upper gastro-intestinal examination showed an ulcerating growth, 2 cm in diameter, in the third portion of the duodenum, and there was a 3 × 4-cm filling defect around the ulceration. Carcinoma of the duodenum was suspected. The results of duodenoscopy revealed a 6 × 7-cm tumour with deep ulceration in the centre of the tumour (*Fig.* 4). Biopsy of the tumour showed a poorly differentiated adenocarcinoma (*Fig.* 5), and primary carcinoma of the duodenum was diagnosed.

An extended pancreatoduodenectomy was performed, with removal of the antrum of the stomach, the duodenum, contiguous lymph nodes near the coeliac axis, fat and lymph nodes near the superior mesenteric artery and vein and lymph nodes over the aorta underlying the third and fourth portions of the duodenum. Reconstruction was accomplished in the same manner as in *Case* 1.

The pathologist reported that sections of the tumour showed a poorly differentiated adenocarcinoma with extension through all layers of the bowel wall, including the serosa. Five of the regional lymph nodes examined showed no involvement.

Three months after discharge the patient was symptom-free and there was no evidence of recurrence.

Discussion

In necropsy studies the incidence of carcinoma of the duodenum is 0·01–0·04 per cent (Eger, 1933; Willis, 1948). It comprises 0·3 per cent of all gastro-intestinal carcinomas and 45–47 per cent of those of the small intestine (Eger, 1933; Hancock, 1970).

Descriptions of the distribution of carcinoma of the duodenum state that 59·2 per cent of the tumours are periampullary and also that supra-ampullary lesions (22·5 per cent) are more common than infra-ampullary (18·3 per cent) (Ebert et al., 1953; Brenner, 1955; Maurer, 1968; Cleator, 1970). By contrast, Resnik and Cooper (1958) have reported 17 per cent as periampullary with the remainder being evenly distributed above and below the ampulla.

The age distribution has its peak in the fifth and sixth decades but the lesion can occur as early as the second decade. Most series report an equal incidence in both sexes (Kenefick, 1972).

The most common symptoms and signs are those of gastro-intestinal obstruction, abdominal discomfort and pain, weight loss and chronic blood loss leading to anaemia. Burgerman et al. (1956), reviewing 31 cases of duodenal carcinoma, found the incidence of symptoms to be as follows: abdominal pain 74 per cent, anaemia 55 per cent, melaena 29 per cent, haematemesis 23 per cent, jaundice 23 per cent, abdominal mass 19 per cent. In the present cases weight loss and anaemia were the main symptoms in *Case* 1, and abdominal pain and weight loss in *Case* 2. Neither patient was jaundiced and the confirmed diagnosis in both cases was infra-ampullary carcinoma. Each case had repeatedly positive occult blood in the stool. This suggested that chronic haemorrhage and iron-deficiency anaemia are the important clinical symptoms. Early clinical diagnosis of carcinoma of the duodenum is extremely difficult, especially for carcinoma in the infra-ampullary region. It relies entirely on suspicion and awareness of the condition. Initial symptoms are vague, and the more severe symptoms such as obstruction, gastro-intestinal haemorrhage and perforation are late features. However, early diagnosis is essential if the poor prognosis is to be improved.

Upper gastro-intestinal examination may not help in diagnosis as its accuracy is limited, and the third part of the duodenum especially is difficult to visualize and may need special positioning. This causes further delay in diagnosis. In a recent report routine upper gastro-intestinal examination diagnosed only about 64·6 per cent of the cases correctly (Sakker and Ware, 1973). In the present series upper gastro-intestinal examination in *Case* 1 revealed the tumour (2 × 3 cm), and in *Case* 2 ulceration in the third part of the duodenum. Usually tumours of the duodenum of more than 1 cm are demonstrable. When this technique is unsatisfactory, hypotonic duodenography is advisable. However, in the present cases the upper gastro-intestinal examinations alone revealed the lesions, although the nature of the growths could be confirmed by biopsy.

The development of duodenoscopy should help to diagnose carcinoma of the duodenum by direct visualization, photography of the tumour of the duodenum and biopsy. Duodenoscopy will not only distinguish carcinoma of the duodenum from pancreatic carcinoma, ampullary carcinoma and secondary tumour from adjacent organs but also diagnose these abnormalities at an early stage. In the present series diagnosis of primary carcinoma of the duodenum was confirmed by duodenoscopy and biopsy. It is suggested that duodenoscopy and biopsy are of great value in obtaining an accurate diagnosis before operation.

The choice of treatment depends on the extent of the lesion and the general condition and age of the patients. Pancreatoduodenectomy should be performed when feasible as this gives the best results. Operability of this disease has increased from 50 per cent (Resnik and Cooper, 1958) to 93·4 per cent (Serrano and Mcpeak, 1966; Sakker and Ware, 1973) and resectability of the tumour has also increased from 41 per cent (Serrano and Mcpeak, 1966) to 61·7 per cent (Sakker and Ware, 1973). However, the 5-year survival rate in this disease is still low. In *Case* 1 a radical operation was carried out satisfactorily because there was no extension of the carcinoma through the duodenum and no lymph node metastases. In *Case* 2, the tumour was larger than in *Case* 1 but a radical operation was performed because there was no invasion of the carcinoma through the duodenum and no lymph node metastases. Both patients have been well and free of symptoms for 14 months and 3 months respectively.

Conclusions

In the diagnosis of carcinoma of the duodenum careful radiological examination is a very important procedure. Duodenoscopy and biopsy are the most reliable methods to confirm the duodenal pathology.

The cases reported here emphasize that duodenoscopy and biopsy are of great value in confirming the diagnosis and in understanding the state of the disease before operation. It is suggested that duodenoscopy and biopsy will increase the resectability and the 5-year survival rate. In the near future the early detection of carcinoma of the duodenum by this method may become practical.

References

BRENNER R. L. (1955) Primary carcinoma of duodenum: report of 15 cases. *Gastroenterology* **29**, 189–198.

BURGERMAN A., BAGGENSTOSS A. H. and CAIN J. C. (1956) Primary malignant neoplasmas of the duodenum, excluding the papilla of Vater: a clinicopathologic study of 31 cases. *Gastroenterology* **30**, 421–431.

CARTESE A. F. and CORNALL G. M. (1972) Carcinoma of the duodenum. *Cancer* **29**, 1010–1015.

CLEATOR I. G. M. (1970) Carcinoma of the third part of the duodenum. *Br. J. Surg.* **57**, 934–937.

EBERT R. E., PARKHURST G. F., MELENDY O. A. and OSBORNE M. P. (1953) Primary tumors of duodenum. *Surg. Gynecol. Obstet.* **97**, 135–139.

EGER S. A. (1933) Primary malignant disease of duodenum. *Arch. Surg.* **27**, 1087–1108.

HANCOCK R. J. (1970) An 11-year review of primary tumors of the small bowel, including duodenum. *Can. Med. Assoc. J.* **103**, 1177–1179.

KENEFICK J. S. (1972) Carcinoma of the duodenum. *Br. J. Surg.* **59**, 50–55.

MAURER P. (1968) Das Duodenalcarcinom. *Chirurg.* **39**, 527–528.

RESNIK H. L. and COOPER D. R. (1958) Carcinoma of the duodenum: review of the literature from 1948 to 1956. *Am. J. Surg.* **95**, 946–952.

SAKKER S. and WARE C. C. (1973) Carcinoma of the duodenum: comparison of surgery, radiotherapy and chemotherapy. *Br. J. Surg.* **60**, 867–872.

SERRANO J. F. and MCPEAK C. J. (1966) Primary neoplasma of the duodenum. *Surgery* **59**, 199–202.

WARREN K. W., CATTELL R. B., BLACKBURN J. P. and NORA P. F. (1962) A long-term appraisal of pancreatics duodenal resection for peri-ampullary carcinoma. *Ann. Surg.* **155**, 653–662.

WILLIS R. A. (1948) *Pathology of Tumours.* London, Butterworths, p. 411.

SURGICAL RESEARCH SOCIETY

The Winter Meeting of the Surgical Research Society will be held at St Mary's Hospital, London, on 9 and 10 January 1976. For further information please contact the Honorary Secretary: Professor P. R. F. Bell, Department of Surgery, Leicester General Hospital, Gwendolen Road, Leicester.

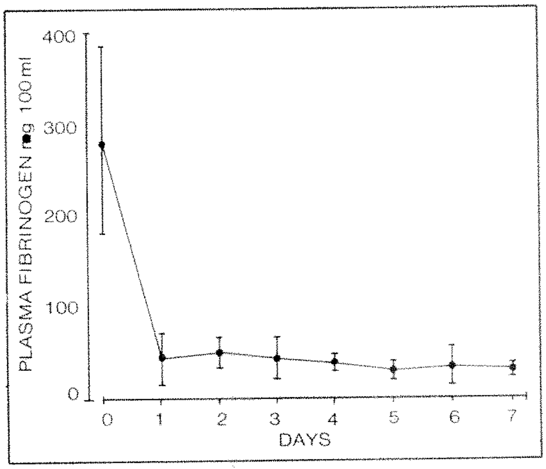
Sensitivity, when you most need it.
REGENT
DISPO
SURGEONS' GLOVES
at the centre of surgery
LR Industries Limited North Circular Road London E4 8QA
Regent Dispo is a registered trade mark

Thackray Electro-Medical products for the '70's incorporate the latest features in engineering and design, manufactured to a high standard by our technicians, renowned for quality throughout the surgical world. Each of the products illustrated fulfils particular requirements essential to the surgeon. Every item comprises high quality components, being thoroughly and comprehensively tested before leaving our factory.

For further information please contact:

Chas. F. Thackray Limited, P.O. Box

A new concept in the control of occlusive vascular disease.



Mean plasma fibrinogen level ± SD in 9 patients with venous thromboses. Arvin 2 units/kg body weight intravenously every 12 hours. From Pitney WR. (1971). Thromb Diath Haemorrh. 45, 43.

Its name is Arvin.

This unique drug is now available to specialists, for routine anticoagulant therapy, and to researchers into thromboembolic disorders.

Arvin reduces plasma fibrinogen to a level that maintains marked hypocoagulability without serious spontaneous bleeding complications. This desirable effect is achieved through the specificity of Arvin for fibrinogen—other clotting factors are unaffected.

The consistent does-effect relationship of Arvin allows simple and precise methods of control.

On this basis, we recommend Arvin wherever controlled therapeutic defibrination is desirable.

Full prescribing information, and clinical evidence from studies on the broad range of thromboembolic disorders, are available on request.

Arvin
ancrod

controlled therapeutic defibrination.

Berk Pharmaceuticals Shalford, Surrey.

Arvin is a registered trademark

J4591

Your hands are your most important instruments-
it pays to take care of them

The obvious fact that a surgeon's hands are of prime importance to his work was borne in mind when 'Hibiscrub' was formulated. 'Hibiscrub' is designed to keep hands healthy, even after repeated use.

However, the prime importance of a handwash is effectiveness: rapid prolonged bactericidal action against skin bacteria is assured by the presence of the well-proven antiseptic 'Hibitane'.

"These studies have shown that a 4% chlorhexidine detergent solution ['Hibiscrub'] is a potentially outstanding addition to the small list of detergent-disinfectant preparations for the hands of surgeons and nurses, with a greater immediate effect than that obtained with the hexachlorophane or even the iodophor preparations."
British Medical Journal, (1973), 1, 510.

hibiscrub

RAPID BACTERICIDAL SKIN CLEANSER

Contains 'Hibitane' Chlorhexidine Gluconate 4% w/v.

ICI Pharmaceuticals Division
Macclesfield
Cheshire SK10 4TF

THE QUEEN'S AWARD TO INDUSTRY

'Hibitane' and 'Hibiscrub' are trade marks.

PH828

Br. J. Surg. Vol. 62 (1975) 977–981

Clinical features of the degenerate meniscus with the results of meniscectomy

JONATHAN NOBLE*

SUMMARY

A series of 172 patients with an unambiguous diagnosis of horizontal cleavage lesion is reviewed, the average duration of which was 4½ years. Although all the patients complained of pain, night pain and mechanical instability were not invariable. Joint line tenderness was the commonest physical sign. Whereas all but 7 per cent were either 'cured' or 'improved', nearly half the patients had persistent complaints, usually pain. The objective physical findings at review frequently failed to correspond with patients' opinions of their knees. Recovery after meniscectomy may be slow.

In Smillie's (1970a) experience a horizontal cleavage lesion is the commonest single meniscus tear. Reference to other literature regarding meniscus pathology suggests that horizontal cleavage is neglected as a diagnostic entity. Smillie (1970b) has described the typical signs and symptoms, but their incidence has not been quantified. Noble and Hamblen (1975) discovered this lesion in at least one meniscus in 60 per cent of an elderly group of random autopsy subjects, and concluded that not all people possessing such a lesion were likely to have had complaints from it. All patients who were recorded as having had a horizontal cleavage lesion removed in the University Department of Orthopaedic Surgery, Edinburgh, between 1963 and 1968 have been reviewed to determine the incidence of clinical features and to assess the results of meniscectomy.

Patients

One thousand two hundred and twenty-five patients underwent meniscectomy in this department between 1963 and 1968, from whom there were 172 patients with an unambiguous operative diagnosis of horizontal cleavage lesion. This included menisci with a parrot beak tear and horizontal cleavage and also frayed degenerate menisci with gross horizontal tearing. One hundred and fifty-five patients were still available for follow-up, of whom 113 (74 per cent have been recently reviewed for this study (*Table I*). A further 27 returned a questionnaire regarding their pre- and postoperative symptoms, so that we had information from 92 per cent of the available patients, 8 per cent apparently ignoring all communications. Thirteen patients were untraceable or had emigrated, 5 had died before review and in 2 patients review was precluded by further surgery.

Simultaneously, 100 consecutive patients who were admitted for meniscectomy were asked preoperatively if they experienced night pain. Their reply was then correlated with the pathology of the excised meniscus.

Findings

Age and occupation

Fig. 1 shows a predominantly middle-aged series although one-third were below the age of 40 and 2 patients were in their teens. Twenty-eight per cent of the males were coal miners.

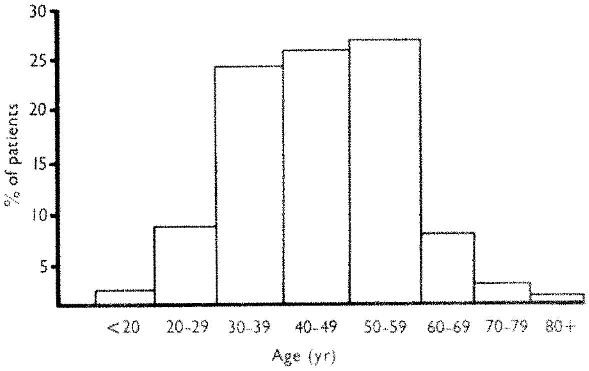


Fig. 1. Age distribution.

Table I: RESULTS OF REVIEW 1969–70 AND 1974

Patients:	Examined	No.: 113 (74%)
	Completed questionnaire	27 (18%)
	Ignored contact	12
	Total available	152 (92%)
	Died before review	5
	Surgery excluded	2
	Untraceable/emigrated	13
	Total unavailable	20
	Total no of patients	172

Duration of follow-up and onset

The duration of follow-up is shown in *Fig.* 2, the overall average for which was 4½ years. The onset of symptoms was insidious in 49 per cent.

Sex and side distribution

In this clinical series the incidence of horizontal cleavage lesions in males and females and on the medial and lateral sides has been compared with the same parameters in the autopsy series (Noble and Hamblen, 1975) (*Fig.* 3). In the clinical study males

---

* University Department of Orthopaedic Surgery, Princess Margaret Rose Orthopaedic Hospital, Edinburgh.

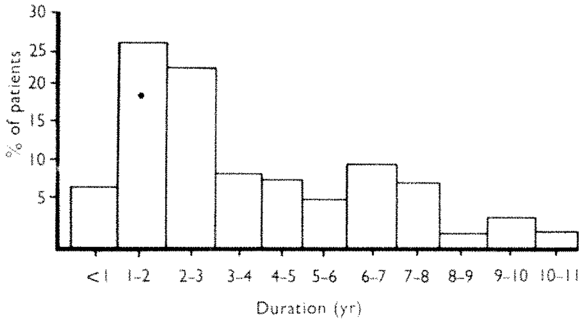


Fig. 2. Duration of follow-up.

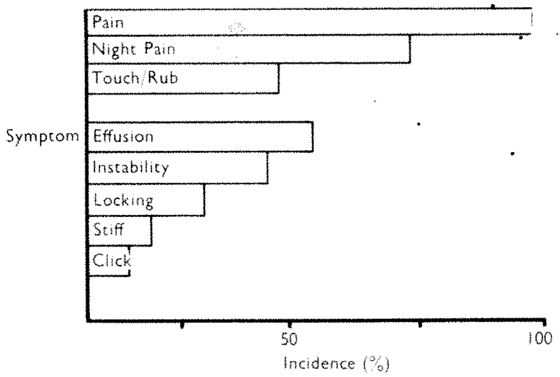


Fig. 4. Incidence of symptoms.

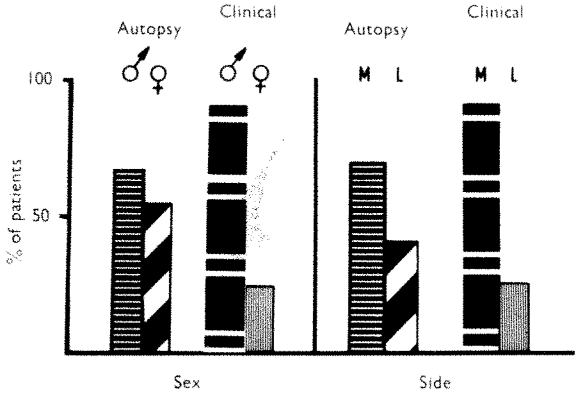


Fig. 3. Sex and side of lesion in autopsy (Noble and Hamblen, 1975) and clinical series. M, Medial; L, lateral.

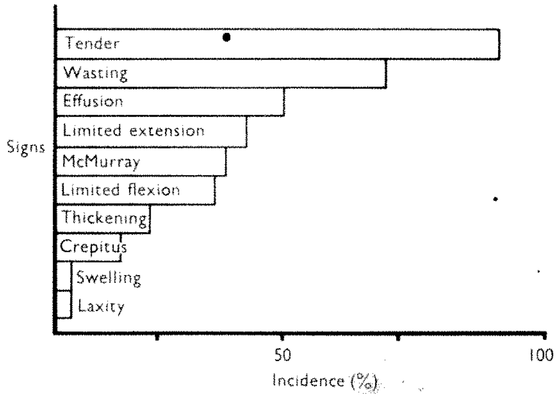


Fig. 5. Incidence of physical signs.

and medial lesions outnumbered females and lateral lesions respectively by 5 : 1, whereas in the autopsy series the male : female ratio approached equality, and the ratio of medial to lateral lesions was only 2 : 1.

Symptoms

The incidence of symptoms is shown in *Fig.* 4, pain being invariable. Seventy per cent complained of night pain, 62 per cent of whom said it was brought on or worsened by their knees touching or rubbing together Two-thirds of these patients separated their knees in bed by means of a pillow. Some patients only had night pain on turning over in bed, or when lying recumbent and 13 per cent put a pillow behind rather than between their knees to keep them in flexion. Fifty-seven per cent mentioned knee swelling, 45 per cent experienced instability or a feeling of insecurity, particularly on walking over uneven ground, and 32 per cent complained of locking.

Two-thirds of the 100 patients questioned just before meniscectomy complained of night pain, including several who were found to have bucket handle tears. Alternatively, not all those who had a horizontal cleavage lesion had previously complained of night pain.

Physical signs

Fig. 5 shows that the commonest physical sign was joint line tenderness, elicited in 86 per cent, whereas the region of the joint line was noted to be thickened in 22 per cent. Two-thirds of the cases had quadriceps wasting and half had an effusion, whilst limitation of extension and/or flexion was recorded in rather less than half the patients.

Results

Almost half of the patients examined or questioned (*Fig.* 6) still had pain, although in most it had been improved by meniscectomy. Twenty-three per cent had night pain, all of whom exhibited joint line tenderness. Sixteen per cent complained of stiffness and another 16 per cent of instability although none complained of locking. One-third of those seen on review had crepitus (*Fig.* 7) although often slight; this was the commonest sign on review. Approximately 20 per cent were noted to have wasting, joint line tenderness, effusion or limitation of flexion and/or extension. Fifteen per cent demonstrated an asymmetrical laxity of the anterior cruciate ligament, which had only been recorded preoperatively in 2 per cent. Twenty-four per cent of those reviewed had an entirely normal knee. However, the objective physical findings did not always match patients' opinions of their knees. One-third of those with an apparently normal knee had complaints, whereas there were other patients who regarded themselves as 'cured' but were found to have significant physical signs.

Although 65 per cent of the patients left hospital in less than 2 weeks, 91 per cent lost more than a month off work following surgery, including several housewives unable to resume full domestic duties. Nine patients, 8 of them coal miners, felt that their knee condition had brought about a change or loss of job.

Seven patients are now dead, this being unrelated to meniscectomy in all but the case of a 56-year-old woman who died of a pulmonary embolus 10 weeks postoperatively. Five patients underwent further surgery. One who is now dead had a high tibial osteotomy and another an arthrodesis 1½ years after meniscectomy from an already degenerate joint. One young man had a patellectomy for osteoarthrosis 4 years after excision of a lateral horizontal cleavage lesion. He still cycles to work at the coal mine, but he required excision of a stitch granuloma, as did one other patient. Recently, a middle-aged man had loose bodies removed from his knee 8 years after meniscectomy.

In summary, 46 per cent regarded themselves as 'cured' and 47 per cent as 'improved' usually 'greatly so'. Five per cent said they were 'the same' and 2 per cent 'worse'. In all but 2 of this group of unimproved patients osteoarthritis was already established but they enjoyed some transient benefit from meniscectomy. The remaining 2, however, were healthy young people, one with evidence of chondromalacia patella and the other with an apparently perfect knee and he played competitive club rugby two or three times a week. Sixty-seven per cent of those who had had night pain said that it was 'cured' and 25 per cent claimed that it was 'improved', while 8 per cent remained 'the same' or 'worse'.

Discussion

Whereas the surgical incidence of these lesions predominates in the middle-aged, this series included 3 teenagers and 5 patients over the age of 70.

The differences relating to sex and side between this clinical series and the reported autopsy subjects (Noble and Hamblen, 1975) for the same type of tear suggests that factors in addition to the possession of the lesion cause symptoms.

Occupation might be a factor to cause gross tearing with associated symptoms from an underlying and much commoner microscopic degenerative process. In Noble and Hamblen's (1975) study such changes were invariably found amongst both macroscopically torn and untorn menisci, and Pfeil (1966) and Zippel (1964) have reported similar findings. It may well be that there is an invariable and therefore 'normal' background of physiological ageing changes which predispose to microscopic tears from laminar shearing forces. If that is the case, then miners could be particularly vulnerable because of the flexion–rotation strains to which they are subject. In half the patients the onset was acute and traumatic, often occurring in coal miners, whose preponderance amongst the males in this series greatly exceeded their prevalence in this region.

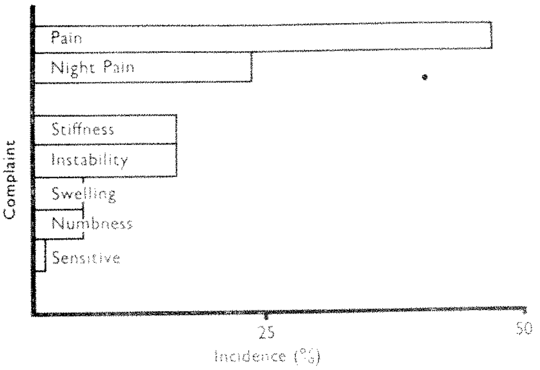


Fig. 6. Incidence of symptoms at follow-up.

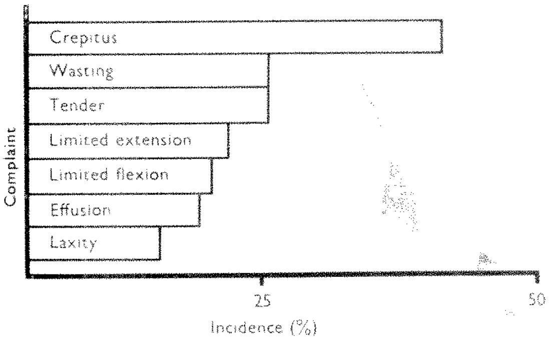


Fig. 7. Incidence of physical signs at follow-up.

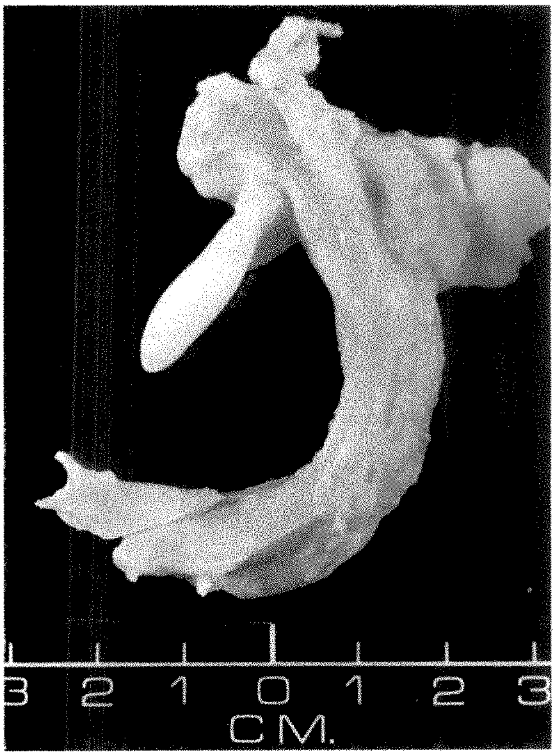


Fig. 8. Horizontal cleavage lesion with polypoid tag.

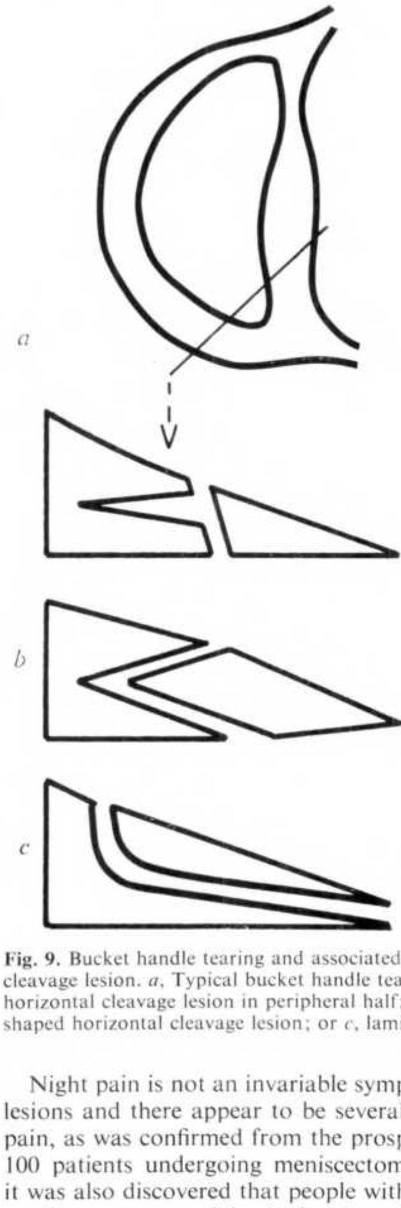


Fig. 9. Bucket handle tearing and associated horizontal cleavage lesion. *a*, Typical bucket handle tear with horizontal cleavage lesion in peripheral half; or *b*, diamond-shaped horizontal cleavage lesion; or *c*, laminar tear.

Night pain is not an invariable symptom with these lesions and there appear to be several types of night pain, as was confirmed from the prospective study of 100 patients undergoing meniscectomy, from which it was also discovered that people with other types of meniscus tear complained of night pain.

Mechanical symptoms and signs, such as locking and mechanical instability, might be explained by the existence of polypoid tags arising from the posterior third of a meniscus which may become trapped between the condyles (*Fig.* 8), or from associated bucket handle tearing, as represented diagrammatically in *Fig.* 9. This shows the several ways it can occur, one of which, the laminar displaced tear, is shown in *Fig.* 10. It may be of practical value to separate the group with only painful symptoms from those who also complained of locking and/or mechanical instability.

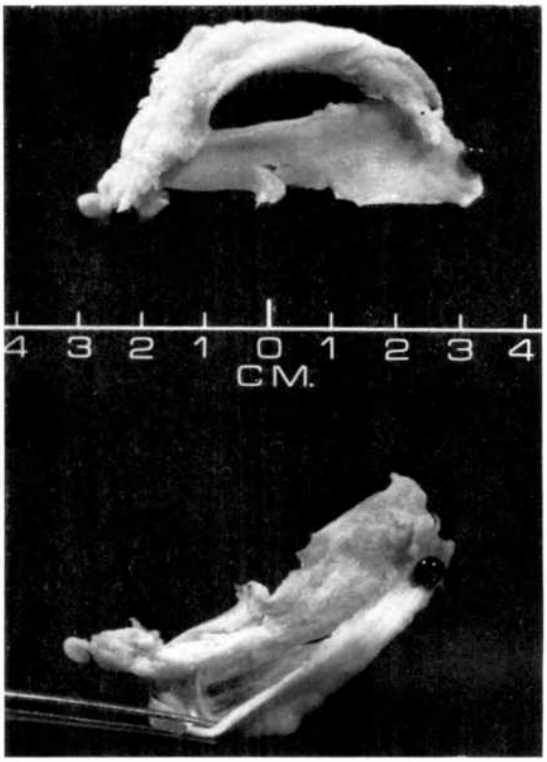


Fig. 10. Photograph of a bucket handle tear and associated laminar lesion.

In 1970 Le Quesne et al. reported 80 per cent lasting relief from juxtameniscal pain by means of cortisone injections in a small series of patients including those with degenerative menisci. Such simple therapy may be advisable in the first instance in all those whose complaints exclude mechanical symptoms. Miller et al. (1958) reported relief from knee pain in nearly two-thirds of a large series by various injections of which the placebo effect seemed to be important. Bentley and Goodfellow (1969), however, have warned of the dangers of intra-articular hydrocortisone injections.

Conclusions

1. The horizontal cleavage lesion probably exists much more commonly than symptoms arising from it. Therefore, other factors must be involved in the production of symptoms.

2. Although night pain is a cardinal symptom, it is not invariable. There are different types of night pain and their significance varies.

3. Although the results of meniscectomy were usually good, less than half the patients were completely relieved of pain and only two-thirds had their night pain completely abolished. Recovery may be slow, so that surgery is not to be undertaken lightly, and patients' response to surgery may be capricious.

4. Alternatively, there may be a group of middle-aged patients, hitherto labelled as 'osteoarthritic', with mechanical symptoms from a degenerate meniscus due to a polypoid tag or associated bucket handle tear who might benefit from a meniscectomy. Surgery should be primarily offered to this group.

5. Local anaesthetic with or without extra-articular cortisone injection may be worth trying in patients with predominantly painful symptoms.

Acknowledgements

Grateful thanks are due to all the consultant staff of Princess Margaret Rose Orthopaedic Hospital who have allowed their patients and material to be studied.

Special thanks are due to Professor J. I. P. James and Professor D. L. Hamblen who suggested and supervised the study.

References

BENTLEY G. and GOODFELLOW J. W. (1969) Disorganisation of the knees following intra-articular hydrocortisone injection. *J. Bone Joint Surg.* (*Br.*) **51**, 498.

LE QUESNE M., BENASASSON M., KEMMER C. and AMOUROUX J. (1970) Painful juxtameniscal areas in certain arthropathies of the knee and their treatment by juxtameniscal cortisone infiltration. *Ann. Rheum. Dis.* **29**, 689.

MILLER J. M., WHITE J. and NORTON T. H. (1958) The value of intra-articular injections in osteoarthritis of the knee. *J. Bone Joint Surg.* (*Br.*) **40**, 636.

NOBLE J. and HAMBLEN D. L. (1975) The pathology of the degenerate meniscus lesion. *J. Bone Joint Surg.* In the press.

PFEIL E. (1966) Meniscusläsion und Alter. *Z. Orthop.* **102**, 308.

SMILLIE I. S. (1970a) *Injuries of the Knee Joint*, 4th ed. Edinburgh, Churchill-Livingstone, p. 41.

SMILLIE I. S. (1970b) *Injuries of the Knee Joint*, 4th ed. Edinburgh, Churchill-Livingstone, p. 79.

ZIPPEL H. (1964) Meniscusschäden und Meniscus Verletzungen. Eine Untersuchung 1360 Meniscus Operationen. *Arch. Orthop. Unfallchir.* **56**, 236.

Br. J. Surg. Vol. 62 (1975) 982–986

Pressure measurements beneath below-knee amputation stump bandages: elastic bandaging, the Puddifoot dressing and a pneumatic bandaging technique compared

P. A. ISHERWOOD, J. C. ROBERTSON AND A. ROSSI*

SUMMARY

Elastic wrap bandaging is unreliable and dangerous in terms of pressure and pressure distribution (tourniquet effect). The Puddifoot dressing is safe and is less likely to produce a tourniquet effect. The range of pressures it produces is low—possibly too low to achieve ideal moulding or oedema control. A pneumatic bandage achieved a relatively narrow range of pressures between capillary and arteriolar blood pressures. It minimized tourniquet effects and differences between skilled and unskilled bandagers. It is sufficiently promising to merit development.

THE role of bandaging in amputation stump management is a controversial subject, and likely to remain so. A bandage may be required to act as a dressing that, despite movement, can stay on for hours, days or even weeks, to hold tissues in the control of stump oedema or to mould amputation stumps to facilitate prosthetic fitting. It should be cheap, disposable, easily sterilized and permit easy access and observation. Above all it must be safe even when applied by unskilled, ill-informed, geriatric and handicapped users to tissues which may be compromised by ischaemia, metabolic or neurological diseases or recent surgery. A stump bandage will exert pressure on the skin, yet it is not known how much pressure the skin and subcutaneous tissues can withstand and for how long. Pressures at isolated points beneath applied stump bandages do not appear to have previously been recorded in the literature.

The work of Müller et al. (1954) with erythema time gives some idea of how the pressure/time factors operate on non-weight-bearing skin in the absence of shearing strains. They maintained that sustained pressures in excess of 0·04 kg/cm^2 (25 mm Hg) are potentially harmful. Spiro et al. (1970), in a series of femoral vein blood flow measurements during varying degrees of lower limb compression, discovered that a sustained pressure of above 15 mm Hg decreased flow. Provided that bandage pressure does not exceed intravascular hydrostatic pressure, bandaging will limit the formation of oedema but will not increase the vascular resistance to the detriment of blood flow. Intracapillary pressure varies with posture (Chant, 1972), and in the recumbent position this is exceeded in the lower limb by externally applied pressures of 15–20 mm Hg. As intracapillary pressure varies with dependency, the ideal bandage should provide a graded pressure, which is maximum at the most dependent distal point, decreasing proximally. A hydrostatic bandage devised along these lines has been described elsewhere (Wood, 1968), but despite its advocates (Chant, 1972) is not in general use. Variations in lower limb venous flow, as assessed by radiological dye studies with varying degrees of externally applied pressure, were correlated with distal venous pressure measurements by Hosni et al. (1968), who found that pressures greater than 15–20 mm Hg applied to the popliteal fossa caused a tourniquet pressure effect even when the entire limb was wrapped. They recommended that bandages should stop below the knee joint. Johnson (1972) believed that no dressing with a pressure exceeding 10 mm Hg should be left on overnight. Redhead (1974), however, has applied cycled pressures never dropping below 25 mm Hg to postoperative limbs with benefit.

At present it is rare for a bandager to check clinically the pressures he applies, and an attempt has been made to ascertain the pressure distribution beneath three different types of bandages applied to a series of healed below-knee amputation stumps. Stump bandaging is employed routinely in the rehabilitation of the amputee to control stump oedema and facilitate moulding.

Patients and methods

A series of 21 below-knee amputation stumps of 17 unselected patients of both sexes with vascular, diabetic or neurological disease were studied. All the stumps were considered to be surgically healed but varying in maturity. The patients were studied in the semirecumbent position lying on hospital beds or on a firm couch. The bandages compared were a full length (5 yd) 4-inch wide Rayolast elasticated roll, which is the wrap bandage routinely used in the Limb Fitting Centre of Queen Mary's Hospital, Roehampton, the Puddifoot stump bandage (Puddifoot et al., 1973) and a pneumatic bandage designed by one of us (P. A. I.). The Rayolast bandage was applied as shown in *Fig.* 1 at half-stretch, more firmly at the end of the stump and less at the top. The knee joint was not included

---

* Biomechanics R. and D. Unit, Department of Health and Social Security, and Queen Mary's Hospital, Roehampton, London.

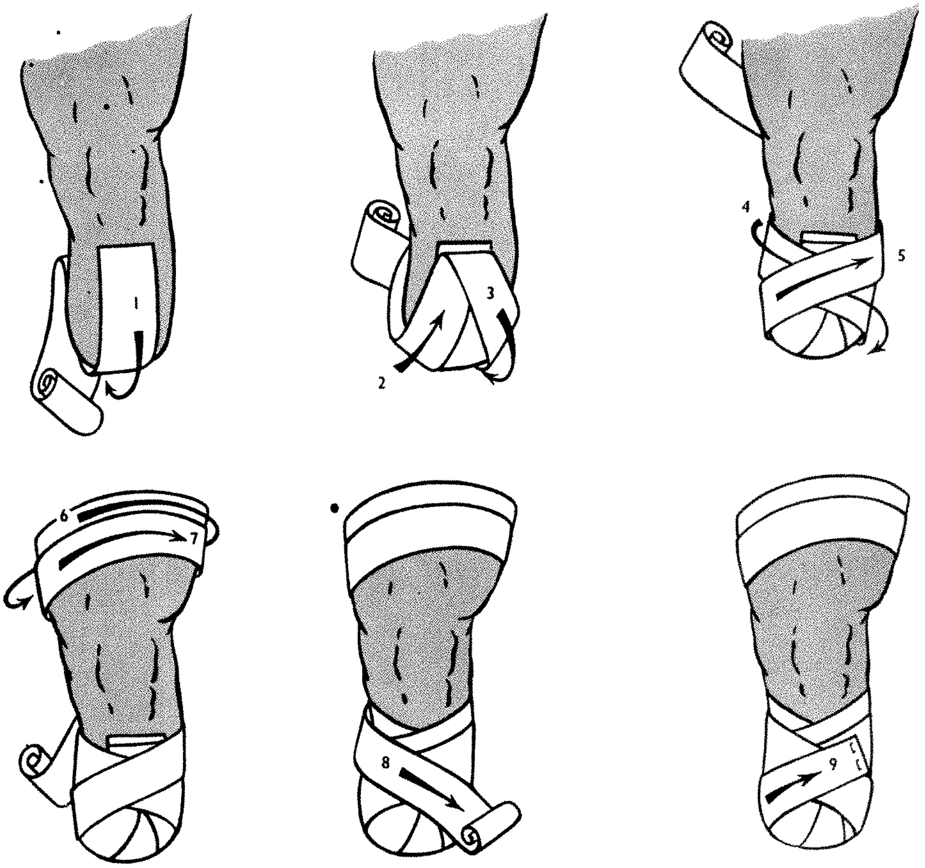


Fig. 1. The important turns of a below-knee stump bandage. Diagonal turns are repeated as often as necessary to cover the stump adequately.

anteriorly to facilitate joint movement, and the wrap was held in place by several loose turns around the thigh just above the patella. This is the approved method of applying this bandage at the Limb Fitting Centre. The Puddifoot dressing and method of application are described elsewhere (Puddifoot et al., 1973). The pneumatic bandage consists of four welded transparent PVC bags of 24 × 6 cm, partially filled with air and sealed. Each bag was wrapped lengthways with its middle portion over the end of the stump, lying side by side along the stump and crossing over each other distally. They were held in place by a Rayolast bandage which was simply wrapped in a circular fashion at about half-stretch around the bags, no particular attempt being made to cover the end of the stump, and held in place by a couple of turns above the knee. The knee joint was not covered anteriorly. Before any bandages were applied six pressure sensors were attached to the stump in the following positions: anterior tibial tubercle, head of the fibula, medial side of the knee at a point opposite the head of the fibula and the centre of the popliteal fossa. The remaining two sensors were applied at the end of the stump, one directly over the end of tibia and the other over the adjacent posterior soft tissue. The apparatus is shown in *Fig*. 2. When the pressure in the system exceeds the forces compressing the flattened sensor, the plastic envelope balloons, so parting the contacts and switching off the light. The pressure is then reduced at a rate of 2 mm/sec until the light comes on again,

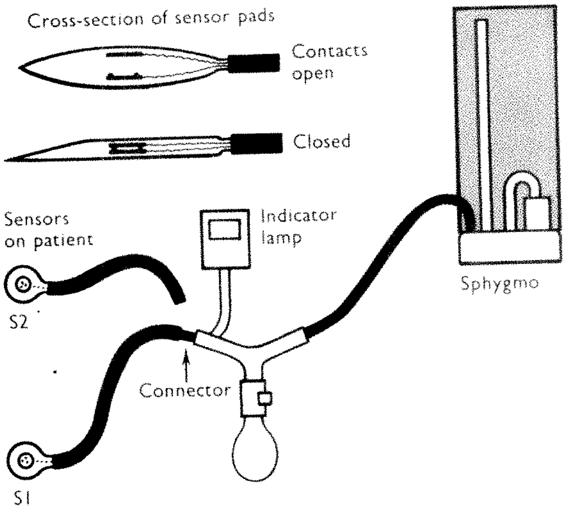


Fig. 2. The pneumatic/electric pressure sensor.

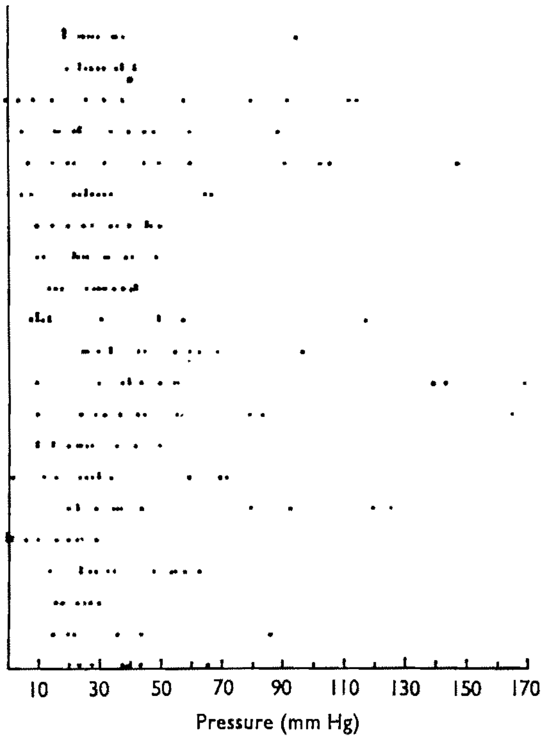


Fig. 3. Range of pressures recorded for Rayolast bandages. ○, Skilled bandager. ●, Unskilled bandager.

indicating the pressure between the surfaces. The apparatus was tested against known heights of water at a range of temperature varying from ambient to above body temperature (23–38 °C). The maximum deviations from the calculated values were +2·1 and −3·1 mm Hg. It was found that readings below 11 mm Hg were unreliable. Bandages were applied by staff skilled in bandage application including physiotherapists, nursing staff trained in the care of amputees and two of the authors (J. C. R. and A. R.). Pressures beneath the bandages after skilled application were compared with those of unskilled bandagers, i.e. the amputees themselves, occasionally assisted by their relatives. Measurements were taken immediately after bandage application over a 5-minute period. Twenty-two series of pressure recordings were measured with the stump resting on the bed and nine series with the stump elevated, the patient supporting the thigh.

Results

Pressure readings from each site were measured with an adapted sphygmomanometer machine. Above 11 mm Hg the apparatus was accurate to within 3 mm Hg, but although readings below this level were considered individually unreliable they were included in the statistical treatment of results. *Figs.* 3–5 show the range of pressures recorded for each of the three bandages, illustrating the pressures developed at each sensor site for each of the 21 stump applications by both skilled and unskilled bandagers with the stump

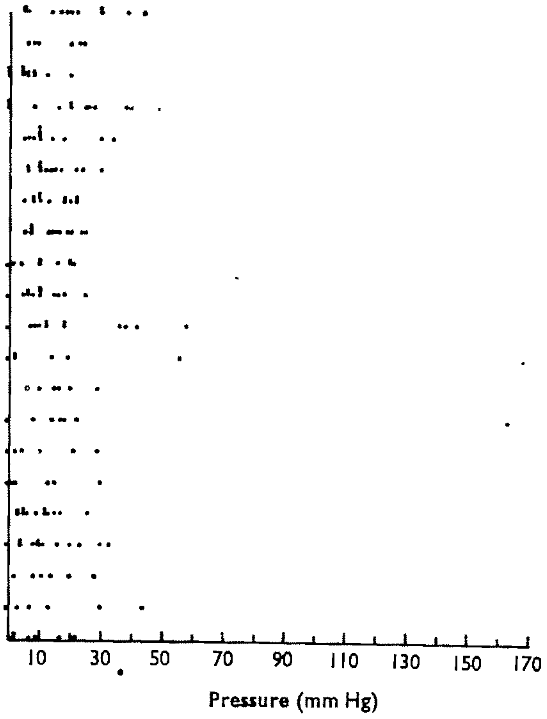


Fig. 4. Range of pressures recorded for Puddifoot bandages.

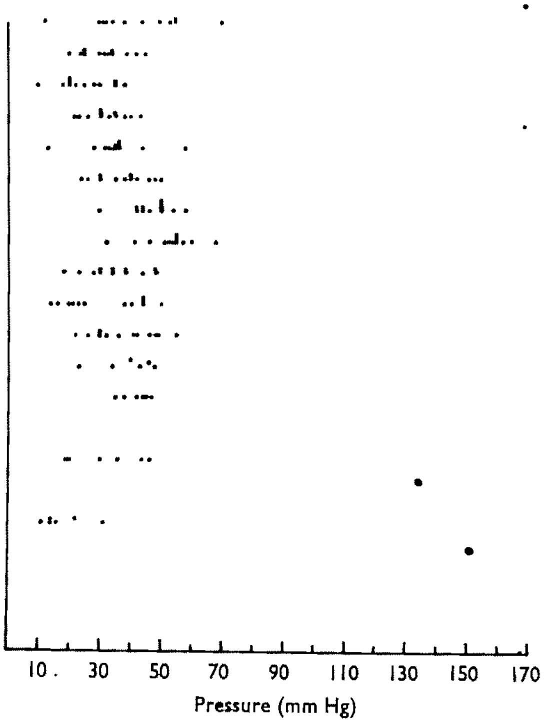


Fig. 5. Range of pressures recorded for pneumatic bandages.

resting on a bed or couch. The means of the pressures recorded from each individual sensor site were calculated for the three types of bandage. The calculations were made for the series of 21 skilled and unskilled applications with the stump resting, and similarly for the 9 skilled applications with the stump elevated. These results were recorded to assess and compare the presence of any tourniquet effect (*Table I*). In a second series of 22 Rayolast applications to 7 below-knee amputation stumps of 5 patients, two additional sensors were positioned proximally on either side of the tibial tubercle to assess more fully the distribution of proximal ring pressure. Readings were taken immediately after bandage application by a random selection of skilled and unskilled bandagers and the means of the pressure recordings from each site were calculated (*Table II*).

Discussion

As can be seen from *Figs*. 3–5 the greatest range of pressures is beneath the Rayolast, and the majority of the highest readings in this group follow unskilled applications. This is not surprising as variations in stump diameter at different levels may result in a variable number of turns of the bandage to be applied, and so portions of the stump may have more bandage coverings than others. Considerable practice is needed to judge bandage tension during application and few bandagers follow Fegan's (1973) advice to feel the tension in the bandaged tissues. Chavatzas and Jamieson (1974), in measurements of skin blood pressure, recorded levels of 59–73 mm Hg for healthy pretibial skin and levels of 17–50 mm Hg for pretibial skin of patients with popliteal stenosis. Two in 13 of the pressures recorded beneath Rayolast bandages at similar sites were in excess of 59 mm Hg. This bandage was comfortable, but although easily applied by the patients themselves, was not always applied in the approved manner despite repeated instruction. The Puddifoot dressing has a much narrower pressure scatter distribution and pressures were generally much lower than those under the Rayolast. Almost half of the readings, however, were below 11 mm Hg, and 1 in 11 was zero. As a supportive dressing it was comfortable when on, although it tended to be painful during the process of application in the early post-operative period, but with practice was easily applied by most patients. Clinically, it has been shown to aid moulding and oedema control (Puddifoot et al., 1973), despite the low pressure readings obtained. The pneumatic bandage also shows less pressure scatter than the Rayolast, and while 1 in 18 of the pretibial pressure measurements was 60 mm Hg, only 1 was less than 11 mm Hg. This was a predicted result as the pressure applied to the bags by the Rayolast at the sides of the stump is fairly evenly transmitted throughout the bag to the end of the stump. The bandage was comfortable, with a little practice easily applied by the amputee and did not tend to slip.

A tourniquet effect was considered to have been produced when the mean of the lowest proximal sensor pressure readings was greater than that of either of the distal sensors. Using this criterion the maximal tourniquet effect was seen with the stump resting after unskilled application of Rayolast (*Table I*). A tourniquet effect was still recorded following skilled application, although this was less and disappeared following elevation of the stump. This might be anticipated from the reduction in pressure on the popliteal fossa following elevation. No tourniquet effect was demonstrated with the Puddifoot dressing and there appears to be an appreciable difference between the higher distal end and the lower proximal pressures. Apart from a minimal tourniquet effect following elevation, there was no such effect with resting measurements following application of the pneumatic bandage. This range is probably more effective than that of the Puddifoot dressing for oedema control, but is uncomfortably close to skin arteriolar blood pressure in arteriopaths.

From the second series of 22 Rayolast applications with the sensors dispersed proximally, the highest mean was calculated from recordings at the tibial tubercle, as might be expected (*Table II*). An interesting finding is the low mean pressure calculated at the medial, anteromedial and anterolateral sites relative to the popliteal fossa with the stump resting. This may be due, at the medial site, to the relatively soft subcutaneous tissue, and for the latter two sites, to a

Table I: CALCULATED MEAN PRESSURES AT EACH SENSOR SITE FOR EACH TYPE OF BANDAGE

Sensor site	Calculated mean pressure (mm Hg) Skilled, leg resting	 Unskilled, leg resting	 Skilled, leg elevated
Rayolast			
Medial	29	43	27
Popliteal	34	51	18
Tibial tubercle	59	72	57
Fibula head	29	39	31
End hard	24	26	22
End soft	27	23	26
Puddifoot			
Medial	5	10	6
Popliteal	14	15	5
Tibial tubercle	9	11	13
Fibula head	8	9	7
End hard	21	22	12
End soft	23	23	15
Pneumatic			
Medial	35	31	42
Popliteal	43	43	38
Tibial tubercle	43	35	51
Fibula head	40	33	40
End hard	37	35	41
End soft	42	35	39

Table II: CALCULATED MEAN PRESSURES AT EACH PROXIMAL SENSOR SITE FOR SKILLED AND UNSKILLED BANDAGERS USING RAYOLAST

Sensor site	Calculated mean pressure (mm Hg)
Medial	36
Popliteal	39
Tibial tubercle	67
Fibula head	35
Anterior medial	26
Anterior lateral	35

bridging effect, the sensors being in a hollow part of the proximal circumference. Possibly these sites provide exits for lymphatic drainage as important as the popliteal region in the below-knee amputee.

In conclusion, we feel that Rayolast bandaging is potentially dangerous, especially if applied by the unskilled, that the Puddifoot dressing exerts too low a pressure to the stump for ideal moulding and that the pneumatic bandaging technique produces a higher, more evenly distributed therapeutic range of pressures, is safe and worthy of further clinical trial.

Acknowledgements

We wish to thank Dr I. H. M. Curwen, Mr K. P. Robinson, Mr A. G. Rutter, Dr M. Vitali and the surgeons of the Limb Fitting Centre, Roehampton, for their kindness in allowing us to approach their patients. Without the help of Miss B. Davies and Miss C. Van der Ven and the support of the nursing staff of Queen Mary's Hospital this study would not have been completed.

The views expressed by P. A. I. are his own and not necessarily the official views of the Department of Health and Social Security.

References

BOURNE I. H. J. (1974) Vertical drainage of oedema in treatment of leg ulcers. *Br. Med. J.* **2**, 581–583.

CHANT A. D. B. (1972) The effects of posture, exercise, and bandage pressure on the clearance of ^{24}Na from the subcutaneous tissues of the foot. *Br. J. Surg.* **59**, 552–555.

CHAVATZAS D. and JAMIESON C. (1974) Measurement o skin blood pressure. *Lancet* **1**, 711–712.

FEGAN W. G. (1973) Bandaging the lower limb. *Nurs. Times* 23 August, pp. 1079–1080.

HOSNI E. A., XIMENES J. O. C. and HAMILTON F. G. (1968 Pressure bandaging of the lower extremity *JAMA* **206**, 2715–2718.

JOHNSON H. D. (1972) Mechanics of elastic bandagin (Correspondence). *Br. Med. J.* **3**, 767–768.

MAY B. J. (1964) Stump bandaging of the lower extremity amputee. *J. Am. Phys. Ther. Assoc.* **44** 808–814.

MÜLLER E. A. and VETTER K. (1954) The effect o pressure loads upon blood supply to the skin *Arbeitsphysiologie* **15**, 295–304.

PUDDIFOOT P. C., WEAVER P. C. and MARSHALL S. A (1973) A method of supportive bandaging fo amputation stumps. *Br. J. Surg.* **60**, 729–731.

REDHEAD R. (1974) Personal communication.

SPIRO M., ROBERTS V. C. and RICHARDS J. B. (1970 The effect of externally applied pressure o femoral vein blood flow. *Br. Med. J.* **1**, 719–723

WOOD E. J. (1968) The venous system. *Sci. Am.* **218** 86–96.

Br. J. Surg. Vol. 62 (1975) 987–989

Reviews and notices of books

The Arteries and Veins of the Human Spinal Cord from Birth

G. F. Dommisse, Pretoria. 245 × 185 mm. Pp. 104+vii. Illustrated. 1974. Edinburgh: Churchill Livingstone. £9.

THE classic anatomical descriptions of the vascular anatomy of the spinal cord, commencing with Adamkiewicz in 1881 and followed by many similar studies, would seem to have left little for the anatomist to add. However, G. F. Dommisse finds points to criticize in these previous studies and many discrepancies which have been the stimulus for him to embark on his own dissections.

This is a very thorough study carried out on forty-two cadavers including thirty neonates utilizing a technique of pressure injection of latex complemented in some cases by radiographic analysis employing Micropaque in gelatin. Dissection of arteries and veins from their origin to their termination with the cord *in situ* was carried out with a microscope and with photographic reproduction. Measurement of the diameter of the anterior and twin posterior longitudinal arterial channels and their feeder vessels was made and recorded at all levels and the findings in the neonates were compared with those in the adult. Thirty colour plates illuminate these dissections very vividly.

The author puts forward the view that in order to provide an adequate and equalized perfusion pressure in the small vessels penetrating the spinal cord there is an elaborate system of anastomostic channels arranged in three situations: on the cord itself, consisting of arcades between the main longitudinal trunks, around the theca extradurally, forming links between the segmental arterial vessels, and thirdly in the extravertebral tissue planes.

This study confirms many of the already well-known anatomical features, in particular the vulnerability of the thoracic segment of the cord deriving from the narrowness of its anterior spinal vessel and the paucity and fine calibre of its feeder arteries. On the other hand, the author points out the great variations in the normal vascular supply and emphasizes that the artery of Adamkiewicz may arise at any level from the fourth dorsal to the second lumbar and that purely on its anatomical situation no feeder vessel to the spinal cord can be disregarded.

The book fills in some gaps in knowledge of the vascular anatomy of the cord and will take its place with other detailed studies of the past. It will be of interest to the anatomist, the pathologist and to the surgeon operating in this hazardous field.

VALENTINE LOGUE

China Medicine as we saw it

Edited Joseph R. Quinn. 230 × 150 mm. Pp. 430+xii. 1974. Bethesda, Md: US Department of Health, Education and Welfare. No price given.

THIS is a delightfully readable book on Chinese medicine in 1974. The authors cover many topics such as general medicine, surgery, public health and nursing. It is, of course, impossible in such a short book to go into great depth on each subject, but there is sufficient detail to give an accurate insight into China's many medical problems, as well as many of her medical successes.

There are four chapters on traditional Chinese medical practice and mixed traditional and Western practice, which describe herbal remedies, acupuncture and acupuncture anaesthesia and reattachment of limbs, as practised in Shanghai. In the public health section the training and work of the 'barefoot doctor' are described. There is an excellent chapter on applied microbiology by a microbiologist who was born in China and who was able to communicate expertly with the Chinese.

This book contains something for everyone who is interested in Chinese medical practice, or indeed in medical practice in countries outside the United Kingdom. There are, unfortunately, political references and ideas in this book, but the influence of politics on medicine in China makes this imperative.

This should be regarded as a book for bedtime reading, rather than an authoritative textbook.

IAN CAPPERAULD

Atlas of the Battered Child Syndrome

J. M. Cameron and L. J. Rae, London. 245 × 185 mm. Pp. 90+ix. Illustrated. 1975. Edinburgh: Churchill Livingstone. £8·50.

THIS short book has been compiled by a forensic pathologist and a radiologist with a contribution from an ophthalmologist, Dr Alan Mushin. At atlas should be judged on its comprehensiveness and the pertinence, clarity and accuracy of its illustrations. These criteria are met successfully in the radiological chapter but other aspects are neither as well covered nor portrayed. The atlas will be of interest to all who are involved with abused children but is primarily intended for doctors who are responsible for the clinical recognition of the syndrome. The differential diagnosis of the radiographic appearances is fully considered and well illustrated, although some mention might have been made of the comparative rarity of congenital syphilis and infantile scurvy. It is surprising that the differential diagnosis of bruises is not discussed because the exclusion of natural causes of bleeding is of considerable clinical and legal importance.

Criticism of the brief, superficial account of the general features of the battered child syndrome and its management is perhaps misplaced. Nevertheless it is unfortunate that speculative figures regarding prevalence and mortality are reiterated, and unconfirmed statistics about recurrence rates are quoted. Children's departments disappeared with the establishment of 'generic' social service departments, while the authors omit the recommended and now largely followed procedures set out by area review committees which place upon the case conference the major role in deciding management.

The book is well produced and the illustrations are of excellent quality. It should find a place on the shelves of every X-ray department but will not be as useful to those dealing with wider aspects of the problem. At £8·50 it seems a somewhat costly production.

THOMAS E. OPPE

Biochemical Values in Clinical Medicine

Robert Duncan Eastham, Newcastle upon Tyne. Fifth edition. 175 × 100 mm. Pp. 237. 1975. Bristol: John Wright. £2.

THIS is the fifth edition of an old favourite, and it is a measure of the success of this book that it has gone through five editions, three reprintings and several foreign editions since it first appeared in 1960. Basically, it is a description of normal ranges for biochemical values in clinical medicine with notes on conditions that affect the performance and the evaluation of the tests and references to the relevant literature. The items are arranged in alphabetical order with the origins of the test material, but are cross-indexed by means of a comprehensive index of subjects at the back of the book. The value of the whole compilation is enhanced by presenting it with a firm cover in a size that fits comfortably into the pocket of a white coat. House surgeons must find it invaluable in the day-to-day care of their patients, but it is also a most convenient, and as far as I can judge accurate, source of information for more senior clinicians as well. This book is excellent value for money.

MICHAEL HOBSLEY

The Etiology of Human Breast Cancer

A. N. Papaioannou, Athens. 240×165 mm. Pp. 228, with 2 illustrations. 1974. Berlin: Springer-Verlag. DM.56.

This is an excellent book and its arrival on the oncology scene is timely. The past few years have produced a wealth of information and speculation concerning the aetiology of human mammary cancer. In this book the author meticulously sifts and analyses all the available evidence and presents his conclusions to the reader in a clear and concise manner.

The author looks first at endocrine considerations and in some ways this is the most provocative part of the story. To quote the author: 'Endocrine factors play an unquestionable, clearcut and fundamental role in experimental breast carcinogenesis.' The evidence in humans is less convincing, but nevertheless many of the factors which undoubtedly influence the relative risk of developing the disease have an endocrine basis. The author makes a very reasoned evaluation of these factors and gives due prominence to the excellent international epidemiological studies of MacMahon and his colleagues.

Chapters 2 and 3 deal with genetic and viral considerations respectively. The former is full of interesting detail, much of it anecdotal. The latter has a more scientific flavour and provides a thoughtful account of a subject which has interested research workers for many decades.

In the fourth and last major chapter of the book the author devotes disproportionate space to immunological considerations, and this is perhaps understandable in view of his own special interests, but the welcome objectivity of the previous chapters is lost as a result. The list of references at the end of this particular chapter is formidable and many are irrelevant to the main theme of the book.

The concluding section deals with a number of miscellaneous factors which may be involved in the aetiology of breast cancer. Of particular interest is a short but intriguing examination of the role of 'psychological stress' in carcinogenesis.

This book is a welcome addition to the already vast literature on mammary cancer and is unreservedly recommended to all who have an interest in the subject.

IAN BURN

Radiology of Bone Diseases

George B. Greenfield, Chicago. Second edition. 210×280 mm. Pp. 667+xvi. Illustrated. 1975. Oxford: Blackwell Scientific Publications. £27·50.

In the second edition of this most valuable and useful book on the differential diagnosis of bone disease, Dr Greenfield has greatly expanded the text, brought the topic up to date and added a new chapter on arthritides. The author has adhered to the concept of presenting his material according to radiological features of the various conditions, clearly describing each entity in some detail, profusely illustrating it and adding helpful basic clinical, biochemical and pathological information.

The main sections of the book include a general description of an analytical approach to bone radiology, and loss of bone density, including osteoporosis, osteomalacia, hyperparathyroidism and other entities. There is a comprehensive chapter on alterations of bone texture, an extensive description of lesions affecting the epiphyseal region and an equally comprehensive section on changes in size and shape of bone. There is a very helpful chapter on the cardinal radiographic features which deals very fully with the main diagnostic appearances of specific conditions. Bone tumours are dealt with in a section on solitary lesions. There is a useful chapter on soft tissue appearances and finally a very comprehensive section on joint disease.

The part of the book dealing with metabolic bone diseases has been completely rewritten and a great deal of new information has been presented on bone changes in renal disease. There is a fully illustrated description of the various types of bone dysplasia, which are well annotated and tabulated.

As in the first edition, the large number of illustrations are of high quality, well chosen and used as a key to interpretation with clear, descriptive captions. Each chapter carries its own bibliography, which is very extensive, bringing the radiological literature well up to date.

The book is eminently readable, a mine of information, and although expensive it is nevertheless a valuable addition to one's library. It will certainly be of great help to orthopaedic surgeons, radiologists and all who are interested in bone disease. Dr Greenfield has done a great service to the speciality of radiology in producing this monumental text which can be highly recommended in every respect.

R. E. STEINER

Advances in Surgery, Volume 8

Edited R. M. Zollinger, Columbus, Ohio. 230×155 mm. Pp. 333+xiv. Illustrated. 1974. London: Lloyd-Luke. £13·50.

This volume deals with a number of important topics where significant change has taken place in surgical practice. It would be difficult to criticize the scholarly review on the surgical treatment of duodenal ulcer by Professor Goligher or the section on hepatic resection by William P. Longmire. The sections on biliary atresia, the surgical approach to nutritional problems and the management of malignant melanoma are perhaps more controversial, but nevertheless provide a great deal of useful information and much food for thought.

There are two excellent sections, one on the effect of halogen anaesthetics on liver metabolism and the immune response and the other on the contributions of immuno-assay to surgery, both of which provide full information on two rather complex changes which affect the management of surgical patients.

The final sections on problems in the intensive care unit and the treatment of wound failure would be of interest to all surgeons.

This book continues to maintain the reputation of its predecessors in providing the surgeon with up-to-date information on topics of general interest.

C. G. CLARK

Clinical Embryology for Medical Students

Richard S. Snell, Washington. Second edition. 185×255 mm. Pp. 481. Illustrated. 1975. Boston: Little, Brown and Co. $12.50 paper, $17.50 cloth.

The first edition of this book in 1972 drew attention to the value of embryology during the student's clinical studies, particularly in relation to congenital abnormalities. The text and its accompanying line drawings provided the essentials of developmental anatomy in an attractive, agreeable way and appealed to the student. The extra 120 pages in the second edition are accounted for by the inclusion of many excellent photographs of congenital abnormalities and by the introduction of a series of clinical problems or exercises at the end of each chapter. In attempting these, the student is expected to test his knowledge of embryology in the clinical context and thereby appreciate its relevance. To derive the full benefit of the scheme, however, it will be necessary to mix embryology with clinical study (or vice versa) in far greater measure than most curricula allow at present.

JOHN MCKENZIE

Stress Fractures

Michael Devas, London. 195×250 mm. Pp. 240+viii. Illustrated. 1975. Edinburgh: Churchill Livingstone. £15.

This monograph represents a very personal and unique experience of several hundred stress fractures and avulsions which the author has described from 'purely' clinical and radiographic standpoints. It began over 15 years ago when the Stress Fracture Bureau at the Middlesex Hospital was set up. There are examples from almost every long and short mature bone of the human skeleton, and all are well illustrated and discussed. Even the horse and the greyhound are shown to have their problems of a similar nature. Biopsy material is naturally very limited and this makes it difficult to add to present day knowledge about the aetiology or indeed aetiologies of these conditions. Under the heading of 'Epilogue' Mr Devas considers very carefully the effects of muscle contraction, and osteoporosis, and their interaction. He also emphasizes that a great deal of experimental work has yet to be done to demonstrate why cellular and hence structural failure has occurred.

The literature has been thoughtfully reviewed and such a grouping for this relatively rare pathology is most helpful.

R. B. DUTHIE

Pediatric Orthopedic Nursing

Nancy E. Hilt and E. William Schmitt, Atlanta, Georgia. 254 × 175 mm. Pp. 248 + xviii, with 301 illustrations. 1975. London: Henry Kimpton. £6·15.

THIS is a really splendid book. The entire field of nursing care of the orthopaedic child is covered in a practical manner without neglecting the emotional problems which are encountered when a child undergoes prolonged surgical attention. The text is highly informative and the illustrations are clear and concise. It may be read with pleasure from cover to cover or can be used as a reference book. It will be found invaluable for teaching nurses. So often textbooks for nursing and paramedical staff have a patronizing tone, but these authors show that it is possible to be simple and instructive without being condescending. This book will, in my opinion, become the standard reference book on paediatric orthopaedic nursing in the foreseeable future. It cannot be commended too highly.

LIPMANN KESSEL

Abdominal Operations. Volumes 1 and 2

Edited R. Maingot. Sixth edition. 250 × 180 mm. Vol. 1: pp. 1220 + xxix; Vol. 2: pp. 2264 + xxiii. Illustrated. 1975. Hemel Hempstead, Herts: Prentice-Hall International. £46·75.

THE sixth edition of this famous work is a worthy successor to previous editions and Rodney Maingot is to be congratulated on drawing contributions from so many distinguished authorities. Descriptions of most of the operations performed by alimentary surgeons are interlaced with discussions of basic principles, sections on physiological and pathological aspects, methods of investigation, historical notes, etc. As a comprehensive text, sensibly presented in two volumes, it is well worth having if your work is mainly in the abdomen and you have not already acquired publications that cover essentially the same field. However, it is atrociously expensive even by present day standards and I doubt if the surgical registrar or Fellowship candidate should—or could—buy it; he would undoubtedly be glad to find it in his hospital library as a superb source of reference on practical and theoretical matters.

Having thus recommended it, I cannot refrain from some criticisms which might be considered for a further edition in a few years. Monographs are all the rage, but I think there will continue to be a place for major 'spectaculars' such as this.

Some subjects must be included and others expanded. For example, proximal gastric vagotomy receives scant attention; the trans-sphincteric approach to the rectum deserves a full description; prolapse of the rectum merits a more thorough exposition; as fissure-in-ano is dealt with, there seems no reason to exclude haemorrhoids; prevention of deep vein thrombosis is worthy of more than three lines.

As a text largely devoted to technique, the avoidance of excessively dogmatic statements is remarkable, and the policy that led to this must be sustained vigorously.

Now to relative trivialities. References are dealt with in different ways in different chapters which is wrong. There seems to be a schizophrenia about whether to use the English or American spelling of such words as haematemesis, colour and anaesthetized, and the common bile duct becomes the choledochus occasionally. To convert inches to centimetres seems reasonable, but it is surely impossibly precise to describe an incision as 7·62 cm from the pyloric sphincter—why not go metric throughout anyway? Some of the illustrations are poor because of excessive shading or detail, and one is frankly silly—we do not need a line drawing to show a surgeon with a hand in an abdomen doing a laparotomy! It also seems out of place to go into such detail as when a patient may get up 'for bedmaking'—particularly when the advice is out-of-date. Despite these blemishes, it is an excellent book—if you can afford it.

ALAN G. COX

Digestive Surgery. Proceedings of the Second World Congress of Collegium Internationale Chirurgiae Digestivae

Edited L. F. Hollender and G. D'Onofrio. 240 × 170 mm. Pp. 969 + xxxii. Illustrated. 1974. Padua: Piccin Medical Books. $60.

THIS long book of approximately one thousand pages comprises the Proceedings of the Second World Congress of Collegium Internationale Chirurgiae Digestivae, held in Strasbourg in June 1972. The volume is divided into sections on the physiology and surgery of the oesophagus and hiatal hernia, the stomach and duodenum, the small intestine, the colon, the rectum and anus, the bile ducts, the pancreas, portal hypertension, etc. As might be expected, some of the contributions are now rather 'old hat', but it is useful to have so many valuable papers collected into one volume. The quality of the contributions is inevitably rather uneven but the general standard is high. It is perhaps invidious to pick out any particular papers for special mention, but there is the expected rash of communications on selective proximal/highly selective/parietal cell vagotomy and an interesting account by G. Holle et al. on the changes in the parietal cell mass after selective proximal vagotomy for gastric ulcer. Kronberger contributes a vigorous defence of gastric resection for chronic peptic ulcer, sentiments which echo those of McKeown in this country and Ochsner from the United States. De Miguel has an interesting paper showing how diarrhoea diminishes as the types of vagotomy become more refined. Brückner and his colleagues from Munich report interesting work on the effect of sympathectomy on pepsin secretion in cats with gastric fistulation. The fascinating data on Crohn's disease from Birmingham presented by J. Alexander-Williams et al. will by now be familiar to most British surgeons. There are fine accounts of the treatment of chronic pancreatitis and of portal hypertension from experts in these fields. Altogether, this is a stimulating publication which should be present in medical libraries, but which one would hesitate to recommend for purchase by the individual surgeon.

DAVID JOHNSTON

Lessons of Leucotomy

Edited Ashley Robin and Duncan Macdonald. 215 × 137 mm. Pp. 100, with 7 illustrations. 1975. London: Henry Kimpton. £2·25.

THE senior editor of this book is noteworthy in that he is one of the few psychiatrists who has paid attention to the need for an adequate control population with which to compare the results of prefrontal leucotomy. He himself, in his study from Runwell Hospital, found that his group of patients derived little benefit. The editors have had an almost impossible task in comparing the results on patients with different diagnoses undergoing different kinds of operation, and there is much evidence, though little of it as yet published, which shows that lesions are by no means always placed in the intended areas. The book contains a considered discussion of the methodology involved in a proper controlled trial and ends with a plea for some adequately controlled trials. It is to be hoped that such trials will indeed be carried out, for the occasional dramatic improvement seems far more than can be due to chance. For examples of this kind of improvement and for the various ill effects that may follow operation there is still no better study and certainly no more entertaining one than Partridge's *Prefrontal Leucotomy* (1950, Oxford, Blackwell). The present volume will encourage a more critical attitude in the future by those concerned with this operation. Neurosurgeons have with stereotaxis increased the accuracy of the lesions that they can produce; it is now the psychiatrists who must play their part.

R. T. C. PRATT

Br. J. Surg. Vol. 62 (1975) 990–1008

Index to Volume 62

Abdomen, acute, appraisal of peritoneal lavage in diagnosis of, 119
Abdominal aortic and iliac aneurysms, false, 734
  approach for ligation of bleeding oesophageal varices, 108
  cancer surgery, is 'second look operation' justified in suspected recurrences after? 830
  lavage in blunt trauma, 121
  stab wounds, selective surgery for, 750
  surgery, prophylactic interparietal povidone-iodine in, 792
  tuberculosis: demonstration of tubercle bacilli in tissues and experimental production of hyperplastic enteric lesions, 610
Abdominoperineal resection for cancer of rectum and rectosigmoid, factors influencing local recurrence after, 727
Abdominoscrotal hydrocele, 629
Abscess, subphrenic, in children, 305
Abtahi F. S. and Djahanguiri B.: Decreased incidence of indomethacin-induced gastric ulceration in rats by bile duct diversion, 113
Acid-citrate-dextrose solution, effect of heparin and of, on screen filtration pressure of blood in experimental hypotension, 713
Acute abdomen, appraisal of peritoneal lavage in diagnosis of, 119
  appendicitis, significance of faecoliths in diagnosis of, 535
  appendicitis, suspected, assessment of value of white cell count in management of, 906
  cholecystitis, 697
  cholecystitis, controlled clinical trial comparing early with interval cholecystectomy for, 850
  cholecystitis, fatal *Clostridium welchii* septicaemia following, 518
  dermal gangrene, diagnosis, clinical course and treatment of, 364
  gastric erosions, bleeding, management of: role of gastric hypothermia, 221
  pancreatitis, aetiology of hypocalcaemia in, 115
  pancreatitis, prospective study of, 490
Adenomas, parathyroid, localization of, by computer-assisted parathyroid scanning, 553
Adenocarcinoma of rectum, complications of synchronous combined excision for, at St Mark's Hospital, 901
Adenopathy type 1, multiple endocrine, possible parathyroid origin of gastrin in patient with, 313
Adiseshiah M.: Bilateral idiopathic parotid duct strictures, 468
Airan M. C.: *See* Gordon D. L. jt auth.
Alexander-Williams J.: *See* Keighley M. R. B. jt auth., Steinberg D. M. jt auth.
Alho A.: *See* Jäättelä A. jt auth.
Alimentary tract, neoplastic change in duplications of, 269
  tract, nutritional support in management of external fistulas of, 100
Allograft, measurement of immune response to: amino acid incorporation by peripheral white blood cells in man, 863
α-1-Acid glycoprotein, serum, as index of dissemination in breast cancer, 816
Amino acid incorporation by peripheral white blood cells in man: measurement of immune response to allograft, 863
AMP, cyclic, and cortisol, effect of surgical trauma on plasma concentrations of, 441
Amputation, immediate operative fitting of upper limb prosthesis at time of, 634
Amputation stump bandages, below-knee, pressure measurements beneath: elastic bandaging, Puddifoot dressing and pneumatic bandaging technique compared, 982
Anaemia, relationship of, to gastric secretion more than 15 years after vagotomy and gastro-enterostomy, 356
Anaesthesia, general, during early pregnancy, 471
Analgesic abuse in urological practice, 298
Anastomosis, colorectal, comparison of one layer and two layer techniques for, 135
  portocaval, prognosis after: 15-year follow-up, 701
  Roux-en-Y, antrectomy with, in treatment of peptic oesophagitis with stricture, 605
  single layer, after rectosigmoid resection, 239
Anastomotic leak, temporary transcaecal ileal diversion in prevention of, in planned colonic surgery (alternative to proximal colostomy), 243
Angioplasty, extended deep femoral: alternative to femoropopliteal bypass, 340
Andrews B. G.: *See* Robinson K. P. jt auth.
Aneurysms, false abdominal aortic and iliac, 734
Angiography, relationship between ultrasound assessment and, in occlusive arterial disease of lower limb, 64
Angorn I. B.: Oesophagogastrostomy without a drainage procedure in oesophageal carcinoma, 601
Anti-thyroid drugs and L-thyroxine, results of 272 operations with special reference to preoperative treatment with: surgical treatment of thyrotoxicosis, 683
Antrectomy with Roux-en-Y anastomosis in treatment of peptic oesophagitis with stricture, 605
Antrum, motility changes in, after proximal gastric vagotomy, 215
  and pylorus, innervated and intact, importance of, in preventing postoperative duodenogastric reflux and gastritis, 845
Aortic and iliac aneurysms, false abdominal, 734
  reconstruction, hydronephrosis complicating, 344
Aorto-iliac insufficiency, undetected: reason for early failure of saphenous vein bypass grafts for obstruction of superficial femoral artery, 567
  reconstruction with special reference to extraperitoneal approach, 596
Appendicectomy, Fowler–Weir approach to, 303
  incidental, with laparotomy for trauma, 487
Appendicitis, acute, significance of faecoliths in diagnosis of, 535
  perforated, with peritonitis, rabbit model of, 642
  suspected acute, assessment of value of white cell count in management of, 906
Arterial disease, occlusive, of lower limb, relationship between ultrasound assessment and angiography in, 64
Arteriographic exposition of parathyroids, 96
Arteriography, mesenteric, bleeding Meckel's diverticulum diagnosed by, 882
Artery, superficial femoral, reason for failure of saphenous vein bypass grafts for obstruction of: undetected aorto-iliac insufficiency, 567
Ascites, resistant malignant, treatment of, by insertion of peritoneo-atrial Holter valve, 104
  unexplained, pneumatosis cystoides intestinalis with, in Ethiopian patients, 379
Askew A. R.: The Fowler–Weir approach to appendicectomy, 303
Asquith P.: *See* Keighley M. R. B. jt auth.
Atkinson D. W.: *See* Morgan O. S. jt auth.
Atrophic gastritis in gastrectomy specimens, 23
Avikainen V.: *See* Jäättelä A. jt auth.

Bacilli, tubercle, demonstration of, in tissues and experimental production of hyperplastic enteric lesions: abdominal tuberculosis, 610
Bacteraemia associated with burns surgery, 638
Bacteria in flower vase water: incidence and significance in general ward practice, 295
Bacteroides fragilis, wound infections due to, following intestinal surgery, 375
Baddeley R. M.: *See* Keighley M. R. B. jt auth.
Balasegaram M.: Early management of corrosive burns of the oesophagus, 444
Balfour T. W.: *See* Chan P. S. F. jt auth.
Ball J.: *See* Brotherton B. J. jt auth.
Bandages, below-knee amputation stump, pressure measurements beneath: elastic bandaging, Puddifoot dressing and pneumatic bandaging technique compared, 982
Bapna R.: *See* Gupta A. S. jt auth.
Barbezat G. O.: *See* Wheatley I. C. jt auth.
Barr W. T.: *See* Henderson W. J. jt auth.
Barron P. T., Vogelfanger I. J. and Waddell W. G.: Orthotopic liver transplantation utilizing a vascular stapling instrument, 438
Bartzokas C. A., Holley, M. P. and Sharp C. A.: Bacteria in flower vase water: incidence and significance in general ward practice, 295
Bathgate E. M.: *See* Roberts M. M. jt auth.
Baum M.: *See* Roberts J. G. jt auth.
Baxby K. and Johnson R. W. G.: Prediction of kidney viability before transplantation, 810
Beard C. H., Ribeiro C. D. and Jones D. M.: The bacteraemia associated with burns surgery, 638
Beaugie J. M., Belchetz P. E., Brown C. L., Frankel R. J. and Lloyd M. H.: Report of a family with inherited medullary carcinoma of the thyroid and phaeochromocytoma, 264
Bedi B. S.: *See* Murray W. R. jt auth.
Belchetz P. E.: *See* Beaugie J. M. jt auth.
Bell J. R.: *See* Young S. jt auth.
Bell M. S.: Loose bodies in the elbow, 921
Bell P. R. F.: *See* Canavan J. S. F. jt auth.
Below-knee amputation stump bandages, pressure measurements beneath: elastic bandaging, Puddifoot dressing and pneumatic bandaging technique compared, 982
Bennett R. C.: *See* Blamey R. W. jt auth.
Benson E. A.: *See* Page R. E. jt auth.
Bessent R. G.: *See* Citrin D. L. jt auth.
Bile duct, common, removal of retained gallstones from: experience with sodium cholate infusion and Burhenne catheter, 520
  duct diversion, decreased incidence of indomethacin-induced gastric ulceration in rats by, 113
  salts and gallstone disease, 505
Biliary surgery, controlled trial of parenteral prophylactic gentamicin therapy in, 275
Biopsy, operative, of pancreas, 280
Biosynthesis, collagen, in normal and hypertrophic scars and keloid as function of duration of scar, 741
Bladder stone, hanging, formed around Mersilene mesh, 413
Blamey R. W., Bennett R. C., Singer A. M., Nicol R. and Harrison J.: Measurement of the immune response to an allograft: amino acid incorporation by peripheral white blood cells in man, 863
Bleeding acute gastric erosions, management of: role of gastric hypothermia, 221
  oesophageal varices, abdominal approach for ligation of, 108
Blood, effect of heparin and of acid-citrate-dextrose solution on screen filtration pressure of, in experimental hypotension, 713
  flow, gastric mucosal, observations of, using ^{99}Tc^{m} in rat and man, 788
  flow in lower limb, comparison of impedance and strain gauge plethysmography in measurement of, 909
Bloom A. L.: *See* Vajrabukka T. jt auth.
Bloor K. and Cope V.: Complete disappearance of popliteal arterial thromboses in 2 patients, 141
Blumgart L. H.: *See* Citrin D. L. jt auth., Mackenzie R. J. jt auth., Sokhi G. S. jt auth., Vajrabukka T. jt auth.
Boerema anterior gastropexy, survey of results of, for hiatus hernia over 4-year period, 19
Bolton J. P., Craven E. R., Croft R. J. and Menzies-Gow N.: An assessment of the value of the white cell count in the management of suspected acute appendicitis, 906
Bolton P. M.: *See* Rees B. I. jt auth.
Bone D. E.: *See* Watson A. jt auth.
Bone G.: *See* Britton D. C. jt auth.
Bone, Kiel, cervical spinal interbody fusion with, 147
  scan, ^{99}Tc^{m} phosphate, application of, to study of breast cancer, 201
Borrie J. and Lichter I.: Surgical management and problems of heart pacing, 186
Boulos P. B.: *See* ElMasri S. H. jt auth.
Bourke J. B.: *See* Chan P. S. F. jt auth.
Breast cancer, application of ^{99}Tc^{m} phosphate bone scan to study of, 201
  cancer, feasibility of screening for, 804
  cancer, human, immune reaction to: comparison of skin and leucocyte migration tests, 820
  cancer, serum α-1-acid glycoprotein as index of dissemination in, 816
  carcinoma, nitrogen mustard as adjunctive chemotherapy for, 497
  carcinoma of, survival rate of men with, 963
  disease, sex hormones in, 806
  in situ intraduct carcinoma of: long-term follow up, 957
  lymphosarcoma of, 651
  trans-sphenoidal hypophysectomy in disseminated carcinoma of, 85
Brennan T. G.: *See* Rosenberg I. L. jt auth.
Briggs J. D.: *See* Canavan J. S. F. jt auth.
Britton D. C., Bone G., Wright N. A. and Camplejohn R. S.: Measurement of cell production rates in human gastro-intestinal cancer: a guide to treatment, 813
Britton D. C., Gill B. S., Taylor R. M. R. and James O.: The removal of retained gallstones from the common bile duct: experience with sodium cholate infusion and the Burhenne catheter, 520
Britton K. E.: *See* Ell P. J. jt auth.
Brock, Lord: The importance of environmental conditions, especially temperature, in the operating room and intensive care ward, 253
Brock, Lord: Long survival after operation for cancer of the lung, 1
Brock, Lord, Skinner J. M. and Manders J. T.: Observations on peripheral and central temperatures with particular reference to the occurrence of vasoconstriction, 589
Brooke B. N.: *See* King D. W. jt auth.
Brotherton B. J. and Ball J.: Bilateral simultaneous rupture of the quadriceps tendons, 918
Brown C.: *See* George P. jt auth.
Brown C. L.: *See* Beaugie J. M. jt auth.
Browne C. H., Hanson G. C., De Jode L. R. and Roberts P. A.: Rupture of subcapsular haematoma of the liver in a case of eclampsia, 237
Browne M. K.: *See* Thomson J. A. jt auth.
Bruun E.: *See* Efsen F. jt auth.
Bullets, rubber, injuries caused by: report on 90 patients, 480
Burdon D. W.: *See* Keighley M. R. B. jt auth.
Burhenne catheter, experience with sodium cholate infusion and: removal of retained gallstones from common bile duct, 520
Burns, corrosive, of oesophagus, early management of, 444
  surgery, bacteraemia associated with, 638
Bussey H. J. R.: *See* Leppard B. jt auth.
Busuttil A.: *See* Donaldson L. A. jt auth.

Index

Caecal rupture due to colonic ileus, 383
Caecum, presenting clinical picture in perforating carcinoma of: gas gangrene of extremity, 373
Calder J. F.: *See* Reid D. R. K. jt auth.
Cameron E. W. J.: The transdiaphragmatic approach to the heart, 731
Campbell D. J. and Sage R. H.: Thyroid cancer: twenty years' experience in a general hospital, 207
Camplejohn R. S.: *See* Britton D. C. jt auth.
Canavan J. S. F., Briggs J. D. and Bell P. R. F.: Gastric acid secretion following renal transplantation, 737
Cancer, breast, application of ^{99}Tc^{m} phosphate bone scan to study of, 201
  breast, feasibility of screening for, 804
  breast, serum α-1-acid glycoprotein as index of dissemination in, 816
  human breast, immune reaction to: comparison of skin and leucocyte migration tests, 820
  human gastro-intestinal, measurement of cell production rates in: guide to treatment, 813
  of lung, long survival after operation for, 1
  rectal, secondary involvement of penis by, 77
  of rectum and rectosigmoid, factors influencing local recurrence after abdominoperineal resection for, 727
  of stomach, is 'second look surgery' justified in suspected recurrences of? 226
  surgery, abdominal, is 'second look operation' justified in suspected recurrences after? 830
  thyroid, non-surgical treatment of, 769
  thyroid, surgery of, 765
  thyroid: twenty years' experience in general hospital, 207
Carcinoma(s) arising in thyroglossal duct remnant: case reports and review of literature, 689
  breast, nitrogen mustard as adjunctive chemotherapy for, 497
  of breast, survival rate of men with, 963
  of caecum, perforating, presenting clinical picture in: gas gangrene of extremity, 373
  disseminated, of breast, trans-sphenoidal hypophysectomy in, 85
  of duodenum: its preoperative diagnosis, 973
  68, of gallbladder, clinicopathological review of, 26
  in situ, intraduct, of breast: long term follow-up, 957
  inherited medullary, of thyroid and phaeochromocytoma, report of family with, 264
  of large bowel in Sudan, 284
  oesophageal, oesophagogastrostomy without drainage procedure in, 601
  otherwise apparently 'early' mammary, significance of occult skeletal metastases, detected by skeletal scintigraphy, in patients with, 694
  of pancreas and periampullary region: clinical study in district general hospital, 130
  primary, of gallbladder, 33
  secondary, of thyroid gland, 692
Cardiac tamponade, fatal, and other mechanical complications of central venous catheters, 6
Carswell J. W., Cotter J. and Master S. P.: Pancreatic pseudocysts in children: 4 cases from Uganda, 360
Cassar J., Polak J. M. and Cooke W. M.: Possible parathyroid origin of gastrin in a patient with multiple endocrine adenopathy type 1, 313
Cassie G. F.: An incision for *en bloc* nephrectomy, 565
Catecholamines, plasma, in severely injured patients: prospective study on 45 patients with multiple injuries, 177
Catheter(s), Burhenne, experience with sodium cholate infusion and: removal of retained gallstones from common bile duct, 520
  central venous, fatal cardiac tamponade and other mechanical complications of, 6
  intravenous, recognition of infection associated with, 404
Cave F. D.: *See* Charlesworth D. jt auth.
Cavernous haemangioma of frontal bone: case report, 330
Cell production rates, measurement of, in human gastro-intestinal cancer: guide to treatment, 813
Cephaloridine, topical, controlled clinical trial against: povidone-iodine for control of surgical wound infection, 292
Cervical spinal interbody fusion with Kiel bone, 147
Chamberlain J., Housley E. and Macpherson A. I. S.: The relationship between ultrasound assessment and angiography in occlusive arterial disease of the lower limb, 64
Champion H. R.: *See* Gill W. jt auth.
Chan P. S. F., Balfour T. W., Bourke J. B. and Smith P. G.: Peritoneal mesothelioma, 576
Charlesworth D., Harris P. L., Cave F. D. and Taylor L.: Undetected aorto-iliac insufficiency: a reason for early failure of saphenous vein bypass grafts for obstruction of the superficial femoral artery, 567
Charlesworth D., Harris P. L. and Palmer M. K.: Intra-arterial infusion of Solcoseryl: a clinical trial of a method of treatment for pre-gangrene of the lower limb, 337
Charlesworth D.: *See also* Schraibman I. G. jt auth.
Chatterjee A. C.: A rare complication of hydrocele, 891
Chavatzas D. and Jamieson C.: False abdominal aortic and iliac aneurysms, 734
Chemotherapy, adjunctive, nitrogen mustard as, for breast carcinoma, 497
Children, infants and, extrinsic duodenal obstruction in, 125
  pancreatic pseudocysts in: 4 cases from Uganda, 360
  subphrenic abscess in, 305
Cholangiography, operative: reappraisal based on review of 400 cholangiograms, 966
Cholecystectomy, flatulent dyspepsia in patients with gallstones undergoing, 231
  interval, controlled clinical trial comparing early with, for acute cholecystitis, 850
Cholecystitis, acute, 697
  acute, controlled clinical trial comparing early with interval cholecystectomy for, 850
  acute, fatal *Clostridium welchii* septicaemia following, 518
Cholecystogram, negative, in gallbladder disease, 581
Cholecystokinin test: assessment, 317
Chronic hydradenitis suppurativa: report of 9 cases, 394
  relapsing pancreatitis, recurrent pleural effusion in, 560
Citrin D. L., Bessent R. G., Greig W. R., McKellar N. J., Furnival C. and Blumgart L. H.: The application of the ^{99}Tc^{m} phosphate bone scan to the study of breast cancer, 201
Clamp, colostomy/ileostomy construction, 246
Clancy M. T. and O'Briain S.: Fatal *Clostridium welchii* septicaemia following acute cholecystitis, 518
Clarke P. R. R. and Williams H. I.: Ossification in extradural fat in Paget's disease of the spine, 571
Claudication, intermittent, phenol sympathectomy in treatment of: controlled clinical trial, 68
Clendinnen B. G.: *See* McCall I. W. jt auth.
Clips, metal, effect of, on tensile properties of healing skin wounds, 945
Clostridium welchii septicaemia, fatal, following acute cholecystitis, 518
Collagen biosynthesis in normal and hypertrophic scars and keloid as function of duration of scar, 741
Colon, changing pattern of hospital admissions for diverticular disease of, 537
Colonic gas cysts, prolonged symptomatic and radiological remission of, after oxygen therapy, 837
  ileus, caecal rupture due to, 383
  surgery, planned, temporary transcaecal ileal diversion in prevention of anastomotic leak in (alternative to proximal colostomy), 243
Colorectal anastomosis, comparison of one layer and two layer techniques for, 135
Colostomy/ileostomy construction clamp, 246
Common bile duct, removal of retained gallstones from: experience with sodium cholate infusion and Burhenne catheter, 520

Computer-assisted parathyroid scanning, localization of parathyroid adenomas, 553
Condon J. R., Ives D., Knight M. J. and Day J.: The aetiology of hypocalcaemia in acute pancreatitis, 115
Condon J. R., Robinson V., Suleman M. I., Fan V. S. and McKeown M. D.: The cause and treatment of post-vagotomy diarrhoea, 309
Congenital hepatic fibrosis: aspects of diagnosis and surgical management, 621
Cook D. B.: *See* Gill G. V. jt auth.
Cooke W. M.: *See* Cassar J. jt auth.
Cope V.: *See* Bloor K. jt auth.
Corrosive burns of oesophagus, early management of, 444
Cortisol, cyclic AMP and, effect of surgical trauma on plasma concentrations of, 441
Cotter J.: *See* Carswell J. W. jt auth.
Cotton L. T. and Roberts V. C.: Extended deep femoral angioplasty: an alternative to femoropopliteal by-pass, 340
Cottrell K. M.: *See* England P. C. jt auth.
Cowley D. J.: *See* George W. D. jt auth.
Cowley R. A.: *See* Gill W. jt auth.
Coyne S. K.: *See* Gierson E. D. jt auth.
Craig R. D. P., Schofield J. D. and Jackson D. S.: Collagen biosynthesis in normal and hypertrophic scars and keloid as a function of the duration of the scar, 741
Craven E. R.: *See* Bolton J. P. jt auth.
Croft R. J.: *See* Bolton J. P. jt auth.
Crohn's disease, results of surgery for, in Glasgow region, 1961–70, 528
Cudmore R. E.: *See* Gill B. jt auth.
Cuschieri A.: *See* Harrison I. D. jt auth., McArthur P. jt auth.
Cyst(s), colonic gas, prolonged symptomatic and radiological remission of, after oxygen therapy, 837
  epidermoid, polyposis coli and Gardner's syndrome, 387
  hydatid, of liver, intrabiliary rupture of, 885
Cystic thyroid nodules, 205

Dalton G. A.: *See* Robin P. E. jt auth.
Dane T. E. B. and King E. G.: Fatal cardiac tamponade and other mechanical complications of central venous catheters, 6
Das P. and Shukla H. S.: Abdominal tuberculosis: demonstration of tubercle bacilli in tissues and experimental production of hyperplastic enteric lesions, 610
Davidson A. I.: *See* Kyle J. jt auth.
Davies C. J.: A survey of the results of the Boerema anterior gastropexy for hiatus hernia over a 4-year-period, 19
Day J.: *See* Condon J. R. jt auth.
Deep vein thrombosis, postoperative, early detection of: assessment of Doppler ultrasound, physical examination and temperature chart, 182
  vein thrombosis, small doses of subcutaneous sodium heparin in prevention of, after elective hip operations, 348
Degenerate meniscus, clinical features of, with results of meniscectomy, 977
Deitel M.: *See* Kaminsky V. M. jt auth.
Dermal gangrene, acute, diagnosis, clinical course and treatment of, 364
Dhruva A.: *See* Gupta A. S. jt auth.
Diarrhoea, postvagotomy, cause and treatment of, 309
Disseminated carcinoma of breast, trans-sphenoidal hypophysectomy in, 85
Dissemination, serum α-1-acid glycoprotein as index of, in breast cancer, 816
Diversion, temporary transcaecal ileal, in prevention of anastomotic leak in planned colonic surgery (alternative to proximal colostomy), 243
Diverticular disease of colon, changing pattern of hospital admissions for, 537
Diverticulitis, sigmoid, ureteric obstruction due to, 247
Diverticulum, Meckel's bleeding, diagnosed by mesenteric arteriography, 882
Djahanguiri B.: *See* Abtahi F. S. jt auth.
Dog intestine, effect of raising concentration of potassium in blood or intestinal lumen on transport of potassium in, 455
de Dombal F. T.: *See* Goligher J. C. jt auth.
Donaldson L. A. and Busuttil A.: A clinicopathological review of 68 carcinomas of the gallbladder, 26
Dongaonkar P. P.: Hanging bladder stone formed around Mersilene mesh, 413
Doppler ultrasound, physical examination and temperature chart, assessment of: early detection of post-operative deep vein thrombosis, 182
Doran F. S. A. and White M.: A clinical trial designed to discover if the primary treatment of varicose veins should be by Fegan's method or by an operation, 72
Dowling B. L.: *See* Royston C. M. S. jt auth.
Drainage procedure, oesophagogastrostomy without, in oesophageal carcinoma, 601
Dudley H. A. F.: *See* Pardy B. J. jt auth.
Duodenal obstruction, extrinsic, in infants and children, 125
  ulcer, effect of size of gastric outlet on gastric emptying after vagotomy for, 879
Duodenogastric reflux and gastritis, postoperative, importance of innervated and intact antrum and pylorus in preventing, 845
Duodenum, carcinoma of: its preoperative diagnosis, 973
Duplications, of alimentary tract, neoplastic change in, 269
Dutta T. and Vasudevan K.: Gangrene of the tongue following self-application of a rubber band, 956
Dyspepsia, flatulent, in patients with gallstones undergoing cholecystectomy, 231
Dysphagia, postvagotomy, 354

Eclampsia, rupture of subcapsular haematoma of liver in case of, 237
Edwards A. J.: *See* Orr M. M. jt auth.
Edwards J. A. C.: *See* Keighley M. R. B. jt auth.
Effusion, recurrent pleural, in chronic relapsing pancreatitis, 560
Efsen F., Bruun E., Lockwood K. and Hasner E.: Arteriographic exposition of the parathyroids, 96
Eiseman B.: *See* Norton L. W. jt auth.
Elastic bandaging, Puddifoot dressing and pneumatic bandaging technique compared: pressure measurements beneath below-knee amputation stump bandages, 982
Elbow, loose bodies in, 921
Elder J. B.: *See* Taylor T. V. jt auth.
Eley A.: *See* Ross C. F. jt auth.
Ell P. J., Todd-Pokropek A. and Britton K. E.: Localization of parathyroid adenomas by computer-assisted parathyroid scanning, 553
Ellis B. W.: Use of logic-based flow patterns in the investigation and management of surgical disorders, 800
Ellis H. and Jayasekara G.: Is 'second look surgery' justified in suspected recurrences of cancer of the stomach? 226
Ellis H.: Is a 'second look operation' justified in suspected recurrences after abdominal cancer surgery? 830
Ellis H.: *See also* Piggott H. jt auth.
Ellis-Pegler R. B.: *See* King D. W. jt auth.
ElMasri S. H. and Boulos P. B.: Carcinoma of the large bowel in the Sudan, 284
Endocrine adenopathy type 1, multiple, possible parathyroid origin of gastrin in patient with, 313
England P. C., Skinner L. G., Cottrell K. M. and Sellwood R. A.: Sex hormones in breast disease, 806
Enteric lesions, hyperplastic, demonstration of tubercle bacilli in tissues and experimental production of: abdominal tuberculosis, 610
Enteritis, acute segmental ischaemic, in Thailand, 716
Environmental conditions, importance of, especially temperature, in operating room and intensive care ward, 252
  tests of linear flow ventilation for operating theatre, 462

Epidermoid cysts, polyposis coli and Gardner's syndrome, 387
Erosions, bleeding acute gastric, management of: role of gastric hypothermia, 221
Ethanol administration, acute, effect of, on exocrine pancreatic secretion of pig, 707
Evans C., Rashid A., Rosenberg I. L. and Pollock A. V.: An appraisal of peritoneal lavage in the diagnosis of the acute abdomen, 119
Evans M.: *See* Pollock A. V. jt auth.
Everett W. G.: A comparison of one layer and two layer techniques for colorectal anastomosis, 135
Exocrine pancreatic secretion of pig, effect of acute ethanol administration on, 707
Extradural haematomas, bilateral, 397
Extraperitoneal approach, aorto-iliac reconstruction with special reference to, 596

Facial nerve, injury of, during surgery of parotid gland, 401
Faecoliths, significance of, in diagnosis of acute appendicitis, 535
False abdominal aortic and iliac aneurysms, 734
Fan V. S.: *See* Condon J. R. jt auth.
Faris I., Thomson J. P. S., Grundy D. J. and Le Quesne L. P.: Operative cholangiography: a reappraisal based on a review of 400 cholangiograms, 966
Fasciitis, nodular: unusual cause of extradural spinal cord compression, 573
Fegan's method, clinical trial designed to discover if primary treatment of varicose veins should be by, or by operation, 72
Femoral angioplasty, extended deep: alternative to femoropopliteal bypass, 340
  artery, superficial, reason for early failure of saphenous vein bypass grafts for obstruction of: undetected aorto-iliac insufficiency, 567
Femoropopliteal bypass, alternative to: extended deep femoral angioplasty, 340
Fibrosis, congenital hepatic: aspects of diagnosis and surgical management, 621
Fistulas, external, of alimentary tract, nutritional support in management of, 100
Flatulent dyspepsia in patients with gallstones undergoing cholecystectomy, 231
Flow patterns, logic-based, use of, in investigation and management of surgical disorders, 800
Flower vase water, bacteria in: incidence and significance in general ward practice, 295
Fordyce J.: *See* MacKenzie M. jt auth.
Fowler–Weir approach to appendicectomy, 303
Frankel R. J.: *See* Beaugie J. M. jt auth.
Freeman R. and King B.: Recognition of infection associated with intravenous catheters, 404
Frontal bone, cavernous haemangioma of: case report, 330
Frozen section, place of, in practical management of melanoma, 840
Fundus, gastric, case of haemorrhage from volvulus of, 224
Furnival C.: *See* Citrin D. L. jt auth.
Furnival C. M.: *See* Mackenzie R. J. jt auth.
Fyfe T. and Quin R. O.: Phenol sympathectomy in the treatment of intermittent claudication: a controlled clinical trial, 68

Galasko C. S. B.: The significance of occult skeletal metastases, detected by skeletal scintigraphy, in patients with otherwise apparently 'early' mammary carcinoma, 694
Gallbladder, clinicopathological review of 68 carcinomas of, 26
  disease, negative cholecystogram in, 581
  primary carcinoma of, 33
Gallstone(s) disease, bile salts and, 505
  flatulent dyspepsia in patients with, undergoing cholecystectomy, 231
Gallstones retained, removal of, from common bile duct: experience with sodium cholate infusion and Burhenne catheter, 520
Gangrene, acute dermal, diagnosis, clinical course and treatment of, 364
  gas, of extremity: presenting clinical picture in perforating carcinoma of caecum, 373
  of tongue following self-application of rubber band, 956
Gardner's syndrome, epidermoid cysts, polyposis coli and, 387
Gas cysts, colonic, prolonged symptomatic and radiological remission of, after oxygen therapy, 837
  gangrene of extremity: presenting clinical picture in perforating carcinoma of caecum, 373
Gastrectomy specimens, atrophic gastritis in, 23
Gastric acid secretion following renal transplantation, 737
  fundus, case of haemorrhage from volvulus of, 224
  hypothermia, role of: management of bleeding acute gastric erosions, 221
  mucosal blood flow, observations of, using ^{99}Tc^{m} in rat and man, 788
  mucosal resection in treatment of peptic ulcer: 1–10 year clinical follow-up, 608
  outlet, effect of size of, on gastric emptying after vagotomy for duodenal ulcer, 879
  secretion, relationship of anaemia to, more than 15 years after vagotomy and gastro-enterostomy, 356
  tuberculosis, primary: case report, 618
  ulcer, recurrence of, after selective vagotomy and pyloroplasty for chronic uncomplicated gastric ulcer: 5–10 year follow-up, 875
  ulceration, indomethacin-induced, decreased incidence of, in rats by bile duct diversion, 113
  vagotomy, proximal, motility changes in antrum after, 215
Gastrin, plasma, and lower oesophageal sphincter pressure after meals, relationship between changes in, 15
  possible parathyroid origin of, in patient with multiple endocrine adenopathy type 1, 313
Gastritis, atrophic, in gastrectomy specimens, 23
  importance of innervated and intact antrum and pylorus in preventing postoperative duodenogastric reflux and, 845
Gastro-enterostomy, vagotomy and, relationship of anaemia to gastric secretion more than 15 years after, 356
Gastropexy, Boerema anterior, survey of results of, for hiatus hernia over 4-year period, 19
Gastro-intestinal cancer, human, measurement of cell production rates in: guide to treatment, 813
Gaylis H.: Some observations on peripheral venous pressure using a non-invasive technique: a preliminary report, 253
George P., Brown C. and Gilchrist J.: Operative biopsy of the pancreas, 280
George W. D.: Feasibility of screening for breast cancer, 804
George W. D., Cowley D. J., Royston C. M., Glass H. I. and Spencer J.: The effect of the size of the gastric outlet on gastric emptying after vagotomy for duodenal ulcer, 879
Gentamicin therapy, parenteral prophylactic, controlled trial of, in biliary surgery, 275
Gierson E. D., Storm F. K., Shaw W. and Coyne S. K.: Caecal rupture due to colonic ileus, 383
Gilchrist J.: *See* George P. jt auth.
Giles G. R.: *See* Rosenberg I. L. jt auth., Trindade L. M. jt auth.
Gill B. and Cudmore R. E.: Significance of faecoliths in the diagnosis of acute appendicitis, 535
Gill B. S.: *See* Britton D. C. jt auth.
Gill G. V., Prudhoe K., Cook D. B. and Latner A. L.: Effect of surgical trauma on plasma concentrations of cyclic AMP and cortisol, 441
Gill W., Champion H. R., Long W. B., Jamaris J. and Cowley R. A.: Abdominal lavage in blunt trauma, 121

Gillespie G.: *See* Young S. jt auth.
Gilmore O. J. A. and Sanderson P. J.: Prophylactic interparietal povidone-iodine in abdominal surgery, 792
Gland, parotid, injury of facial nerve during surgery of, 401
Glass H. I.: *See* George W. D. jt auth.
Glazer G.: Haemorrhagic and necrotizing pancreatitis, 169
Gloves, surgeons', identification of talc on, and in tissue from starch granulomas, 941
Goligher J. C., Irvin T. T., Johnston D., de Dombal F. T., Hill G. L. and Horrocks J. C.: A controlled clinical trial of three methods of closure of laparotomy wounds, 823
Goligher J. C. and Lintott D.: Experience with 26 reservoir ileostomies, 893
Goligher J. C.: *See also* Hill G. L. jt auth., Irvin T. T. jt auth.
Gordon D. L., Airan M. C., Thomas W. and Seidman L. H.: Parathyroid identification by methylene blue infusion, 747
Grafts, saphenous vein bypass, for obstruction of superficial femoral artery, reason for early failure of: undetected aorto-iliac insufficiency, 567
Gram-negative organisms, experimental study on prevention of infections with: orthotopic liver transplantation, 513
Gram-negative septicaemia in surgical practice, 773
Granulomas, starch, identification of talc on surgeons' gloves and in tissue from, 941
Greaney M. G.: Torsion of the testis: a review of 22 cases, 57
Greig W. R.: *See* Citrin D. L. jt auth.
Griffiths K.: *See* Henderson W. J. jt auth.
Grundy D. J.: *See* Faris I. jt auth.
Gumma of liver, 236
Gunn A. A.: *See* Raine P. A. M. jt auth.
Gupta A. S., Kothari L. K., Dhruva A. and Bapna R.: Surgical sterilization by vasectomy and its effect on the structure and function of the testis in man, 59
Gupta H. K. D.: *See* Rawat S. S. jt auth.
Gupta O. P.: *See* Pendse A. K. jt auth.
Gupta S. D., Tiwari I. N. and Pasupathy N. K.: Cavernous haemangioma of the frontal bone: case report, 330
Gurry J. F.: *See* King D. W. jt auth.
Guthrie T. D.: *See* Scott C. C. jt auth.
Gynaecomastia, 326

Haemangioma, cavernous, of frontal bone: case report, 330
Haematoma(s), bilateral extradural, 397
  subcapsular, of liver, rupture of, in case of eclampsia, 237
Haemobilia, traumatic, 234
Haemorrhage, case of, from volvulus of gastric fundus, 224
Haemorrhagic and necrotizing pancreatitis, 169
Haemorrhoids, internal sphincter and Lord's procedure for, 833
  long term review of results of rubber band ligation of, 144
  nature of, 542
Hakami M. and Mosavy S. H.: Triorchidism with normal spermatogenesis: an unusual cause for failure of vasectomy, 633
Hall T. J.: Bleeding Meckel's diverticulum diagnosed by mesenteric arteriography, 882
Hallux, clawed, results of modified Robert Jones operation for, 651
Halnan K. E.: The non-surgical treatment of thyroid cancer, 769
Halvorsen J. F. and Heimann P.: The continent ileostomy of Kock (ileal intra-abdominal reservoir), 52
Hamer D. B.: Gynaecomastia, 326
Hancock B. D. and Smith K.: The internal sphincter and Lord's procedure for haemorrhoids, 833
Hanson G. C.: *See* Browne C. H. jt auth.
Harris P. L.: *See* Charlesworth D. jt auth.
Harrison I. D., Williams D. F. and Cuschieri A.: The effect of metal clips on the tensile properties of healing skin wounds, 945
Harrison J.: *See* Blamey R. W. jt auth.
Harvey R. F.: *See* McCall I. W. jt auth.
Hasner E.: *See* Efsen F. jt auth.
Heard G. and Hinde G.: Hydronephrosis complicating aortic reconstruction, 344
Heart pacing, surgical management and problems of, 186
  transdiaphragmatic approach to, 731
Heenan P. J.: *See* Skinner J. M. jt auth.
Heimann P. and Martinson J.: Surgical treatment of thyrotoxicosis: results of 272 operations with special reference to preoperative treatment with anti-thyroid drugs and L-thyroxine, 683
Heimann P. *See also* Halvorsen J. jt auth.
Helsby R. and Moossa A. R.: Aorto-iliac reconstruction with special reference to the extraperitoneal approach, 596
Hemithorax, skin-lined, construction of, in pigs, 351
Henderson W. J., Melville-Jones C., Barr W. T. and Griffiths K.: Identification of talc on surgeons' gloves and in tissue from starch granulomas, 941
Hendriks W. D. H.: *See* Schalm S. W. jt auth.
Heparin, effect of, and of acid-citrate-dextrose solution on screen filtration pressure of blood in experimental hypotension, 713
  subcutaneous sodium, small doses of, in prevention of deep vein thrombosis after elective hip operations, 348
Hepatectomy, 70 per cent partial, effect of hepatic ischaemia on liver function and restoration of liver mass after, in dog, 431
Hepatic fibrosis, congenital: aspects of diagnosis and surgical management, 621
  ischaemia, effect of, on liver function and restoration of liver mass after 70 per cent partial hepatectomy in dog, 431
  resection, 421
  resection, postoperative problems and management after, for blunt injury to liver, 189
Hepatogram, radio-isotope, value of, in jaundiced patient, 781
Hernia, hiatus, survey of results of Boerema anterior gastropexy for, over 4-year period, 19
Herniorrhaphy, inguinal, use of vas deferens in, 495
Hickman R.: *See* Terblanche J. jt auth., Wheatley I. C. jt auth.
Hill G. L., Goligher J. C., Smith A. H. and Mair W. S. J.: Long term changes in total body water, total exchangeable sodium and total body potassium before and after ileostomy, 524
Hill G. L., Mair W. S. J. and Goligher J. C.: Cause and management of high volume output salt-depleting ileostomy, 720
Hill G. L.: *See also* Goligher J. C. jt auth.
Himal H. S., Watson W. W., Jones C. W. and MacLean L. D.: The management of bleeding acute gastric erosions: the role of gastric hypothermia, 221
Himal H. S.: *See also* Mzabi R. jt auth.
Hinde G.: *See* Heard G. jt auth.
Hines J. R. and Williams J. S.: Nitrogen mustard as adjunctive chemotherapy for breast carcinoma, 497
Hip operations, elective, small doses of subcutaneous sodium heparin in prevention of deep vein thrombosis after, 348
Hodgkin's disease, role of surgery in management of, 853
Holley M. P.: *See* Bartzokas C. A. jt auth.
Holter valve, peritoneo-atrial, treatment of resistant malignant ascites by insertion of, 104
Hormones, sex, in breast disease, 806
Horrocks J. C.: *See* Goligher J. C. jt auth.
Housley E.: *See* Chamberlain J. jt auth.
Hughes L. E.: The place of frozen section in the practical management of melanoma, 840
Human breast cancer, immune reaction to: comparison of skin and leucocyte migration tests, 820
  gastro-intestinal cancer, measurement of cell production rates in: guide to treatment, 813
Hutchison J.: *See* Thomson J. A. jt auth.

Hydatid cyst of liver, intrabiliary rupture of, 885
Hydradenitis suppurativa, chronic: report of 9 cases, 394
Hydrocele, abdominoscrotal, 629
  rare complication of, 891
Hydronephrosis complicating aortic reconstruction, 344
Hyperparathyroidism, true recurrence of: proposed criteria of recurrence, 556
Hyperplastic enteric lesions, demonstration of tubercle bacilli in tissues and experimental production of: abdominal tuberculosis, 610
Hypertrophic scars, normal and, and keloid, collagen biosynthesis in, as function of duration of scar, 741
Hypocalcaemia, aetiology of, in acute pancreatitis, 115
Hypophysectomy, trans-sphenoidal, in disseminated carcinoma of breast, 85
Hypotension, experimental, effect of heparin and of acid-citrate-dextrose solution on screen filtration pressure of blood in, 713
Hypothermia, gastric, role of: management of bleeding acute gastric erosions, 221

Idiopathic parotid duct strictures, bilateral, 468
Ileal diversion, temporary transcaecal, in prevention of anastomotic leak in planned colonic surgery (alternative to proximal colostomy), 243
Ileostomy(ies)/colostomy construction clamp, 246
  continent, of Kock (ileal intra-abdominal reservoir), 52
  high volume output salt-depleting, cause and management of, 720
  long term changes in total body water, total exchangeable sodium and total body potassium before and after, 524
  26 reservoir, experience with, 893
Ileus, colonic, caecal rupture due to, 383
Iliac aneurysms, false abdominal aortic and, 734
Immune reaction to human breast cancer: comparison of skin and leucocyte migration tests, 820
  response to allograft, measurement of: amino acid incorporation by peripheral white blood cells in man, 863
Impedance and strain gauge plethysmography, comparison of, in measurement of blood flow in lower limb, 909
Imrie C. W. and Whyte A. S.: A prospective study of acute pancreatitis, 490
Incision for *en bloc* nephrectomy, 565
Indomethacin-induced gastric ulceration, decreased incidence of, in rats by bile duct diversion, 113
Infants and children, extrinsic duodenal obstruction in, 125
Infection(s) with Gram-negative organisms, experimental study on prevention of: orthotopic liver transplantation, 513
  recognition of, associated with intravenous catheters, 404
  surgical wound, povidone-iodine for control of: controlled clinical trial against topical cephaloridine, 292
  wound, does choice of suture material affect incidence of? 952
  wound, due to *Bacteroides fragilis* following intestinal surgery, 375
Ingrowing toenail, surgical management of, 407
Inguinal herniorrhaphy, use of vas deferens in, 495
Inherited medullary carcinoma of thyroid and phaeochromocytoma, report of family with, 264
Injury(ies), blunt, to liver, postoperative problems and management after hepatic resection for, 189
  caused by rubber bullets: report on 90 patients, 480
  experimental studies on pathophysiological responses of newborn to, 868
  of facial nerve during surgery of parotid gland, 401
Insufficiency, undetected aorto-iliac: reason for early failure of saphenous vein bypass grafts for obstruction of superficial femoral artery, 567
Intensive care ward, importance of environmental conditions, especially temperature, in operating room and, 252
Intermittent claudication, phenol sympathectomy in treatment of: controlled clinical trial, 68
Intestine, dog, effect of raising concentration of potassium in blood or intestinal lumen on transport of potassium in, 455
Intrabiliary rupture of hydatid cyst of liver, 885
Intracranial pressure, raised, due to spinal tumours: 3 rare cases with probable common mechanism, 92
Intraduct carcinoma, *in situ*, of breast: long term follow-up, 957
Intravenous catheters, recognition of infection associated with, 404
Irvin T. T. and Goligher J. C.: A controlled clinical trial of three different methods of perineal wound management following excision of the rectum, 287
Irvin T. T.: *See also* Goligher J. C. jt auth.
Irving A. D.: *See* Matheson N. A. jt auth.
Irving M.: Introduction to Symposium on Gram-negative Septicaemia, 771
Irving M.: The role of surgery in the management of Hodgkin's disease, 853
Ischaemia, hepatic, effect of, on liver function and restoration of liver mass after 70 per cent partial hepatectomy in dog, 431
Ischaemic enteritis, acute segmental, in Thailand, 716
Isherwood P. A., Robertson J. C. and Rossi A.: Pressure measurements beneath below-knee amputation stump bandages: elastic bandaging, the Puddifoot dressing and a pneumatic bandaging technique compared, 982
Ives D.: *See* Condon J. R. jt auth.

Jäättelä A., Alho A., Avikainen V., Karaharju E., Kataja J., Lahdensuu M., Lepistö P., Rokkanen P. and Tervo T.: Plasma catecholamines in severely injured patients: a prospective study on 45 patients with multiple injuries, 177
Jackson D. S.: *See* Craig R. D. P. jt auth.
Jain G. K.: *See* Rawat S. S. jt auth.
Jamaris J.: *See* Gill W. jt auth.
James O.: *See* Britton D. C. jt auth.
Jamieson C.: *See* Chavatzas D. jt auth.
Jaundiced patient, value of radio-isotope hepatogram in, 781
Jayasekara G.: *See* Ellis H. jt auth.
Jerusalem C.: *See* Schalm S. W. jt auth.
De Jode L. R.: *See* Browne C. H. jt auth.
Johnson P. S.: *See* Morgan O. S. jt auth.
Johnson R. W. G.: *See* Baxby K. jt auth.
Johnston D.: *See* Goligher J. C. jt auth.
Johnston I. D. A.: The surgery of thyroid cancer, 765
Johnston I. D. A.: *See also* Wheldon E. J. jt auth.
Johnston S.: *See* Millar R. jt auth.
Jones C. W.: *See* Himal H. S. jt auth.
Jones D. M.: *See* Beard C. H. jt auth.

Kalbag R. M.: *See* Ramani P. S. jt auth.
Kamino K.: *See* Satake K. jt auth.
Kaminsky V. M. and Deitel M.: Nutritional support in the management of external fistulas of the alimentary tract, 100
Karaharju E.: *See* Jäättelä A. jt auth.
Kataja J.: *See* Jäättelä A. jt auth.
Kato M.: *See* Satake K. jt auth.
Kattan Y. B.: Intrabiliary rupture of hydatid cyst of the liver, 885
Keighley M. R. B., Asquith P., Edwards J. A. C. and Alexander-Williams J.: The importance of an innervated and intact antrum and pylorus in preventing postoperative duodenogastric reflux and gastritis, 845

Volume 62 January 1975 to December 1975 Nos. 1 to 12

The British Journal of Surgery

UNDER THE DIRECTION OF THE FOLLOWING EDITORIAL BOARD

*L. P. LE QUESNE London : *Chairman*
*ROBERT COX London : *Vice-Chairman*
*H. H. G. EASTCOTT London : *Editorial Secretary*†
*C. G. CLARK London : *Assistant Editorial Secretary*

A. S. ALDIS Cardiff
DAVID ANNIS Liverpool
R. ATTARD Malta
M. BALASEGARAM Kuala Lumpur : Malaysia
JOHN BARRON Salisbury
A. K. BASU Calcutta : India
*A. K. BIRT Norwich
K. T. CHAN Singapore
*ALAN G. COX Harrow
SIR THEO CRAWFORD London
*SIR DONALD DOUGLAS Dundee
CHARLES DREW London
H. A. F. DUDLEY London (Surgical Research Society)
D. J. DU PLESSIS Johannesburg : South Africa
R. B. DUTHIE Oxford
J. C. GOLIGHER Leeds
J. W. P. GUMMER London
R. S. HANDLEY London
E. S. R. HUGHES Melbourne : Australia
SIR ANDREW W. KAY Glasgow
*H. E. LOCKHART-MUMMERY London
J. LOEWENTHAL Sydney : Australia
VALENTINE LOGUE London
J. H. LOUW Cape Town : South Africa
SIR IAN MCADAM Kampala : Uganda
A. C. McEACHERN Adelaide : Australia
W. MACKENZIE Edmonton : Canada
AIR COMMODORE J. E. MALCOLM Royal Air Force Medical Service
MAJOR-GENERAL S. E. MIAN Rawalpindi : Pakistan
ERIC NANSON Auckland : New Zealand
R. A. NAVARATNE Colombo : Ceylon
C. B. ONG Hong Kong
J. H. PEACOCK Bristol
J. M. PULLAN London
G. QVIST London
D. H. RANDALL Sheffield
H. D. RITCHIE London
C. P. SAMES Bath
ROBERT SHIELDS Liverpool
D. SLOME London
G. SMITH Aberdeen
RODNEY SMITH London
*M. E. SNELL London
*G. W. TAYLOR London (Association of Surgeons)
H. ORISHEJOLOMI THOMAS Lagos : Nigeria
A. S. TILL Oxford
SURGEON VICE-ADMIRAL J. WATT Naval Medical Service
*R. B. WELBOURN London
*A. W. WILKINSON London
SIR MICHAEL WOODRUFF Edinburgh
W. D. WYLIE London

* Constitute the Editorial Committee
† All correspondence to John Wright & Sons Ltd., Bristol BS8 1EX

JOHN WRIGHT & SONS LIMITED BRISTOL BS8 1EX

THE WILLIAMS & WILKINS CO., BALTIMORE

© John Wright & Sons Ltd and the respective contributors named in the List of Contents 1975

All Rights Reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any other form or by any means electronic, mechanical, photocopying, recording or otherwise without the prior permission of the copyright owner for which application should be made to John Wright & Sons Ltd.

PRINTED IN GREAT BRITAIN BY JOHN WRIGHT & SONS
AT THE STONEBRIDGE PRESS, BRISTOL BS4 5NU

		Page
The management of peptic oesophageal stricture	R. C. N. Williamson	448
The effect of raising the concentration of potassium in the blood or intestinal lumen on the transport of potassium in the dog intestine	Anne Hardy Smith and R. Shields	455
Environmental tests of linear flow ventilation for an operating theatre	The late Charles C. Scott and Thomas D. Guthrie	462
Bilateral idiopathic parotid duct strictures	M. Adiseshiah	468
General anaesthesia during early pregnancy	Leo Strunin, K. Knights, J. M. Strunin and Michael E. Ward	471
Renal transplantation in the unimmunosuppressed pig: an abnormal response	John Terblanche, Rosemary Hickman and C. J. Uys	474
Injuries caused by rubber bullets: a report on 90 patients	R. Millar, W. H. Rutherford, S. Johnston and V. J. Malhotra	480
Incidental appendicectomy with laparotomy for trauma	Lawrence W. Norton, Marna Sweeney and Ben Eiseman	487
A prospective study of acute pancreatitis	C. W. Imrie and A. S. Whyte	490
The use of the vas deferens in inguinal herniorrhaphy	Patrick Sames	495
Nitrogen mustard as adjunctive chemotherapy for breast carcinoma	James R. Hines and John S. Williams	497
Reviews and notices of books		501

Number 7

Review paper

Bile salts and gallstone disease	Colin MacKay	505

Original papers

Orthotopic liver transplantation: an experimental study on the prevention of infections with Gram-negative organisms	S. W. Schalm, D. T. Popescu, D. van der Waay, R. A. F. Krom, W. D. H. Hendriks, J. L. Terpstra and C. Jerusalem	513
Fatal *Clostridium welchii* septicaemia following acute cholecystitis	M. T. Clancy and S. O'Briain	518
The removal of retained gallstones from the common bile duct: experience with sodium cholate infusion and the Burhenne catheter	D. C. Britton, B. S. Gill, R. M. R. Taylor and Oliver James	520
Long term changes in total body water, total exchangeable sodium and total body potassium before and after ileostomy	G. L. Hill, J. C. Goligher, A. H. Smith and W. S. J. Mair	524
Results of surgery for Crohn's disease in the Glasgow region, 1961–70	S. Young, I. S. Smith, J. O'Connor, J. R. Bell and G. Gillespie	528
Significance of faecoliths in the diagnosis of acute appendicitis	B. Gill and R. E. Cudmore	535
The changing pattern of hospital admissions for diverticular disease of the colon	James Kyle and Alan I. Davidson	537
The nature of haemorrhoids	W. H. F. Thomson	542
Localization of parathyroid adenomas by computer-assisted parathyroid scanning	P. J. Ell, A. Todd-Pokropek and K. E. Britton	553
True recurrence of hyperparathyroidism: proposed criteria of recurrence	H. Muller	556
Recurrent pleural effusion in chronic relapsing pancreatitis	Rudra Rasaretnam, A. B. V. Perera and M. Kumarasinghe	560
Xanthogranulomatous pyelonephritis: a report of 2 cases	O. S. Morgan, G. D. Nicholson, P. S. Johnson and D. W. Atkinson	563

Contents

		Page
An incision for *en bloc* nephrectomy	G. F. Cassie	565
Undetected aorto-iliac insufficiency: a reason for early failure of saphenous vein bypass grafts for obstruction of the superficial femoral artery	D. Charlesworth, P. L. Harris, F. D. Cave and Linda Taylor	567
Ossification in extradural fat in Paget's disease of the spine	Patrick R. R. Clarke and H. I. Williams	571
Nodular fasciitis: an unusual cause of extradural spinal cord compression	R. P. Sengupta, S. C. So and R. H. Perry	57
Peritoneal mesothelioma	P. S. F. Chan, T. W. Balfour, J. B. Bourke and P. G. Smith	57
The negative cholecystogram in gallbladder disease	D. R. K. Reid and I. M. Rogers	58
Reviews and notices of books		584

Number 8

Original papers

Observations on peripheral and central temperatures with particular reference to the occurrence of vasoconstriction	Lord Brock, J. M. Skinner and J. T. Manders	58
Aorto-iliac reconstruction with special reference to the extraperitoneal approach	Raymond Helbsy and A. R. Moossa	59
Oesophagogastrostomy without a drainage procedure in oesophageal carcinoma	I. B. Angorn	60
Antrectomy with Roux-en-Y anastomosis in the treatment of peptic oesophagitis with stricture	C. M. S. Royston, B. L. Dowling and J. Spencer	60
Gastric mucosal resection in the treatment of peptic ulcer: a 1–10 year clinical follow-up	R. M. Kirk	60
Abdominal tuberculosis: demonstration of tubercle bacilli in tissues and experimental production of hyperplastic enteric lesions	Pritam Das and H. S. Shukla	61
Primary gastric tuberculosis: a case report	R. E. Page, R. E. Williams and E. A. Benson	61
Congenital hepatic fibrosis: aspects of diagnosis and surgical management	G. S. Sokhi, J. J. Morrice, J. O'D. McGee and L. H. Blumgart	62
Splenic-gonadal fusion	A. K. Pendse, P. N. Mathur, M. M. Sharma and O. P. Gupta	62
Abdominoscrotal hydrocele	B. R. Parekh, G. Reinboth and O. P. Mishra	62
Triorchidism with normal spermatogenesis: an unusual cause for failure of vasectomy	M. Hakami and S. H. Mosavy	63
Immediate operative fitting of upper limb prosthesis at the time of amputation	K. P. Robinson, B. G. Andrews and M. Vitali	63
The bacteraemia associated with burns surgery	C. H. Beard, C. D. Ribeiro and D. M. Jones	63
A rabbit model of perforated appendicitis with peritonitis	D. W. King, J. F. Gurry, R. B. Ellis-Pegler and B. N. Brooke	64
The effect of noxytiolin in experimental peritonitis	D. W. King, J. F. Gurry and B. N. Brooke	64
Results of modified Robert Jones operation for clawed hallux	E. I. M'Bamali	64
Lymphosarcoma of the breast	Charles F. Ross and Arnold Eley	65
Surgical Research Society		65
Obituary: Vincent Zachary Cope		66
Reviews and notices of books		67

Number 9

Original papers

		Page
Whither thyrotoxicosis?	W. Michie	673
Surgical treatment of thyrotoxicosis: results of 272 operations with special reference to preoperative treatment with anti-thyroid drugs and L-thyroxine	Peter Heimann and Jan Martinson	683
Carcinoma arising in thyroglossal duct remnant: case reports and review of the literature	Prakash C. Saharia	689
Secondary carcinoma of the thyroid gland	John A. Thomson, J. S. Kennedy, M. K. Browne and J. Hutchison	692
The significance of occult skeletal metastases, detected by skeletal scintigraphy, in patients with otherwise apparently 'early' mammary carcinoma	C. S. B. Galasko	694
Acute cholecystitis	P. A. M. Raine and A. A. Gunn	697
Prognosis after portocaval anastomosis: a 15-year follow-up	R. Windle and J. H. Peacock	701
The effect of acute ethanol administration on the exocrine pancreatic secretion of the pig	I. C. Wheatley, G. O. Barbezat, Rosemary Hickman and J. Terblanche	707
The effect of heparin and of acid-citrate-dextrose solution on screen filtration pressure of blood in experimental hypotension	B. J. Pardy and H. A. F. Dudley	713
Acute segmental ischaemic enteritis in Thailand	Theodore P. Welch and Somsak Sumitswan	716
Cause and management of high volume output salt-depleting ileostomy	G. L. Hill, W. S. J. Mair and J. C. Goligher	720
Factors influencing local recurrence after abdominoperineal resection for cancer of the rectum and rectosigmoid	A. R. Moossa, P. C. Ree, J. E. Marks, B. Levin, C. E. Platz and D. B. Skinner	727
The transdiaphragmatic approach to the heart	E. W. J. Cameron	731
False abdominal aortic and iliac aneurysms	Demetrios Chavatzas and Crawford Jamieson	734
Gastric acid secretion following renal transplantation	J. S. F. Canavan, J. D. Briggs and P. R. F. Bell	737
Collagen biosynthesis in normal and hypertrophic scars and keloid as a function of the duration of the scar	R. D. Peter Craig, J. David Schofield and David S. Jackson	741
A technique for re-exploration of the saphenofemoral junction for recurrent varicose veins	Arthur K. C. Li	745
Parathyroid identification by methylene blue infusion	Donald L. Gordon, Mohan C. Airan, William Thomas and Leon H. Seidman	747
Selective surgery for abdominal stab wounds	A. Thavendran, A. Vijayaragavan and Rudra Rasaretnam	750
Reviews and notices of books		753

Number 10

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND

Barber's Company Symposium on Malignant Disease of the Thyroid Gland

		Page
The pathology of thyroid malignancy	E. D. Williams	757
The aetiology and diagnosis of malignant tumours of the thyroid gland	J. S. H. Wade	760
The surgery of thyroid cancer	Ivan D. A. Johnston	765
The non-surgical treatment of thyroid cancer	K. E. Halnan	769

Symposium on Gram-negative Septicaemia

Introduction	Miles Irving	772
Gram-negative septicaemia in surgical practice	Adrian Litton	773
Septic shock	I. McA. Ledingham	777

Short papers for the Moynihan Prize and Medal

The value of the radio-isotope hepatogram in the jaundiced patient	A. Watson, D. E. Bone, H. J. Testa and Bruce Torrance	781
Observations of gastric mucosal blood flow using ^{99}Tc^{m} in rat and man	T. V. Taylor, B. R. Pullan, J. B. Elder and Bruce Torrance	788
Prophylactic interparietal povidone-iodine in abdominal surgery	O. J. A. Gilmore and P. J. Sanderson	792
Use of logic-based flow patterns in the investigation and management of surgical disorders	B. W. Ellis	800
Feasibility of screening for breast cancer	W. D. George	804
Sex hormones in breast disease	P. C. England, L. G. Skinner, K. M. Cottrell and R. A. Sellwood	806
Prediction of kidney viability before transplantation	K. Baxby and R. W. G. Johnson	810
Measurement of cell production rates in human gastro-intestinal cancer: a guide to treatment	D. C. Britton, G. Bone, N. A. Wright and R. S. Camplejohn	813

Short papers

Serum α-1-acid glycoprotein as an index of dissemination in breast cancer	J. G. Roberts, J. W. Keyser and M. Baum	816
The immune reaction to human breast cancer: a comparison of skin and leucocyte migration tests	M. Maureen Roberts and Eleanor M. Bathgate	820
A controlled clinical trial of three methods of closure of laparotomy wounds	J. C. Goligher, T. T. Irvin, D. Johnston, F. T. de Dombal, G. L. Hill and J. C. Horrocks	823
Is a 'second look operation' justified in suspected recurrences after abdominal cancer surgery?	Harold Ellis	830
The internal sphincter and Lord's procedure for haemorrhoids	B. D. Hancock and K. Smith	833
Prolonged symptomatic and radiological remission of colonic gas cysts after oxygen therapy	A. P. Wyatt	837
The place of frozen section in the practical management of melanoma	L. E. Hughes	840
The importance of an innervated and intact antrum and pylorus in preventing postoperative duodenogastric reflux and gastritis	M. R. B. Keighley, P. Asquith, J. A. C. Edwards and J. Alexander-Williams	845
Controlled clinical trial comparing early with interval cholecystectomy for acute cholecystitis	P. McArthur, A. Cuschieri, R. A. Sells and R. Shields	850

Number 11

Review paper

		Page
The role of surgery in the management of Hodgkin's disease	Miles Irving	853

Original papers

Measurement of the immune response to an allograft: amino acid incorporation by peripheral white blood cells in man	R. W. Blamey, R. C. Bennett, A. M. Singer, Rita Nicol and J. Harrison	863
Experimental studies on the pathophysiological responses of the newborn to injury	R. A. Little	868
Recurrence of gastric ulcer after selective vagotomy and pyloroplasty for chronic uncomplicated gastric ulcer: a 5–10-year follow-up	Jacinto de Miguel	875
The effect of the size of the gastric outlet on gastric emptying after vagotomy for duodenal ulcer	W. D. George, D. J. Cowley, C. M. Royston, H. I. Glass and J. Spencer	879
Bleeding Meckel's diverticulum diagnosed by mesenteric arteriography	T. J. Hall	882
Intrabiliary rupture of hydatid cyst of the liver	Y. B. Kattan	885
A rare complication of hydrocele	A. C. Chatterjee	891
Experience with 26 reservoir ileostomies	J. C. Goligher and D. Lintott	893
The complications of synchronous combined excission for adenocarcinoma of the rectum at St Mark's Hospital	C. G. Marks and Jean K. Ritchie	901
An assessment of the value of the white cell count in the management of suspected acute appendicitis	J. P. Bolton, E. R. Craven, R. J. Croft and N. Menzies-Gow	906
Comparison of impedance and strain gauge plethysmography in the measurement of blood flow in the lower limb	I. G. Schraibman, D. Mott, G. P. Naylor and D. Charlesworth	909
The surgical cure of primary varicose veins	Stanley Rivlin	913
Bilateral simultaneous rupture of the quadriceps tendons	B. J. Brotherton and J. Ball	918
Loose bodies in the elbow	M. S. Bell	921
Reviews and notices of books		925

Number 12

Original papers

Surgical complications of implanting pacemakers	Harold Siddons and K. Nowak	929
The efficiency of surgical masks of varying design and composition	Louis B. Quesnel	936
Identification of talc on surgeons' gloves and in tissue from starch granulomas	W. J. Henderson, C. Melville-Jones, W. T. Barr and K. Griffiths	941
The effect of metal clips on the tensile properties of healing skin wounds	I. D. Harrison, D. F. Williams and A. Cuschieri	945
How tight should tension sutures be tied? A controlled clinical trial	I. L. Rosenberg, T. G. Brennan and G. R. Giles	950
Does the choice of suture material affect the incidence of wound infection?	G. L. Mouzas and A. Yeadon	952
Gangrene of the tongue following self-application of a rubber band	T. Dutta and K. Vasudevan	956
In situ intraduct carcinoma of the breast: a long term follow-up study	R. R. Millis and G. S. J. Thynne	957
The survival rate of men with carcinoma of the breast	R. W. T. Slack	963
Operative cholangiography: a reappraisal based on a review of 400 cholangiograms	Irvin Faris, James P. S. Thomson, D. J. Grundy and L. P. Le Quesne	966

Contents

		Page
Carcinoma of the duodenum: its preoperative diagnosis	K. Satake, M. Sowa, K. Yamashita, K. Kamino, J. Kinoshita, M. Kato and K. Umeyama	973
Clinical features of the degenerate meniscus with the results of meniscectomy	Jonathan Noble	977
Pressure measurements beneath below-knee amputation stump bandages: elastic bandaging, the Puddifoot dressing and a pneumatic bandaging technique compared	P. A. Isherwood, J. C. Robertson and A. Rossi	982
Reviews and notices of books		987
Index to Volume 62		990

Keighley M. R. B., Baddeley R. M., Burdon D. W., Edwards J. A. C., Quoraishi A. H., Oates G. D., Watts G. T. and Alexander-Williams J.: A controlled trial of parenteral prophylactic gentamicin therapy in biliary surgery, 275
Keloid, collagen biosynthesis in normal and hypertrophic scars and, as function of duration of scar, 741
Kelly M. and Kennedy T.: Motility changes in the antrum after proximal gastric vagotomy, 215
Kennedy J. S.: *See* Thomson J. A. jt auth.
Kennedy T.: *See* Kelly M. jt auth.
Keyser J. W.: *See* Roberts J. G. jt auth.
Kidney viability, prediction of, before transplantation, 810
Kiel bone, cervical spinal interbody fusion with, 147
King B.: *See* Freeman R. jt auth.
King D. W., Gurry J. F. and Brooke B. N.: The effect of noxytiolin in experimental peritonitis, 645
King D. W., Gurry J. F., Ellis-Pegler R. B. and Brooke B. N.: A rabbit model of perforated appendicitis with peritonitis, 642
King E. G.: *See* Dane T. E. B. jt auth.
Kingston R. D. and Windsor C. W. O.: Flatulent dyspepsia in patients with gallstones undergoing cholecystectomy, 231
Kinoshita J.: *See* Satake K. jt auth.
Kirk R. M.: Gastric mucosal resection in the treatment of peptic ulcer: a 1–10 year clinical follow-up, 608
Knight M. J.: *See* Condon J. R. jt auth.
Knights K.: *See* Strunin L. jt auth.
Kock, continent ileostomy of, (ileal intra-abdominal reservoir), 52
Kothari L. K.: *See* Gupta A. S. jt auth.
Krom R. A. F.: *See* Schalm S. W. jt auth.
Kumarasinghe M.: *See* Rasaretnam R. jt auth.
Kyle J. and Davidson A. I.: The changing pattern of hospital admissions for diverticular disease of the colon, 537

Lahdensuu M.: *See* Jäättelä A. jt auth.
Laparotomy for trauma, incidental appendicectomy with, 487
  wounds, controlled clinical trial of three methods of closure of, 823
Large bowel, carcinoma of, in Sudan, 284
Latner A. L.: *See* Gill G. V. jt auth.
Lavage, abdominal, in blunt trauma, 121
  peritoneal, appraisal of, in diagnosis of acute abdomen, 119
Lè Quesne L. P.: *See* Faris I. jt auth.
Ledingham I. McA.: Septic shock, 777
Ledingham I. McA. and Tehrani M. A.: Diagnosis, clinical course and treatment of acute dermal gangrene, 364
Lee N. W.: *See* Ong G. B. jt auth.
Leigh D. A.: Wound infections due to *Bacteroides fragilis* following intestinal surgery, 375
Lepistö P.: *See* Jäättelä A. jt auth.
Leppard B. and Bussey H. J. R.: Epidermoid cysts, polyposis coli and Gardner's syndrome, 387
Leucocyte migration tests, comparison of skin and: immune reaction to human breast cancer, 820
Levin B.: *See* Moossa A. R. jt auth.
Li A. K. C.: A technique for re-exploration of the saphenofemoral junction for recurrent varicose veins, 745
Lichter I.: *See* Borrie J. jt auth.
Liegois H.: *See* Steinberg D. M. jt auth.
Ligation of bleeding oesophageal varices, abdominal approach for, 108
  rubber band, of haemorrhoids, long term review of results of, 144
Limb, lower, clinical trial of method of treatment for pre-gangrene of: intra-arterial infusion of Solcoseryl, 337
  lower, comparison of impedance and strain gauge plethysmography in measurement of blood flow in, 909
Linear flow ventilation, environmental tests of, for operating theatre, 462
Lintott D.: *See* Goligher J. C. jt auth.
Little R. A.: Experimental studies on the pathophysiological responses of the newborn to injury, 868
Litton A.: Gram-negative septicaemia in surgical practice, 773
Liver function, effect of hepatic ischaemia on, and restoration of liver mass after 70 per cent partial hepatectomy in dog, 431
  gumma of, 236
  intrabiliary rupture of hydatid cyst of, 885
  postoperative problems and management after hepatic resection for blunt injury to, 189
  rupture of subcapsular haematoma of, in case of eclampsia, 237
  transplantation, orthotopic: experimental study on prevention of infections with Gram-negative organisms, 513
  transplantation, orthotopic, utilizing vascular stapling instrument, 438
Lloyd M. H.: *See* Beaugie J. M. jt auth.
Lockwood K.: *See* Efsen F. jt auth.
Logic-based flow patterns, use of, in investigation and management of surgical disorders, 800
Long W. B.: *See* Gill W. jt auth.
Lord's procedure for haemorrhoids, internal sphincter and, 833
Lucey J. J.: *See* Maurice-Williams R. S. jt auth.
Lung, cancer of, long survival after operation for, 1
Lymphadenitis, tuberculous peripheral, in Igbos of Nigeria, 323
Lymphosarcoma of breast, 651

Ma M. K. G. and Ong G. B.: Cystic thyroid nodules, 205
McArthur P., Cuschieri A., Sells R. A. and Shields R.: Controlled clinical trial comparing early with interval cholecystectomy for acute cholecystitis, 850
McCall I. W., Harvey R. F., Owens C. J. and Clendinnen B. G.: Relationship between changes in plasma gastrin and lower oesophageal sphincter pressure after meals, 15
McGee J. O'D.: *See* Sokhi G. S. jt auth.
MacKay C.: Bile salts and gallstone disease, 505
McKellar N. J.: *See* Citrin D. L. jt auth.
MacKenzie M., Fordyce J. and Young D. G.: Subphrenic abscess in children, 305
Mackenzie R. J., Furnival C. M., O'Keane M. A. and Blumgart L. H.: The effect of hepatic ischaemia on liver function and the restoration of liver mass after 70 per cent partial hepatectomy in the dog, 431
McKeown M. D.: *See* Condon J. R., jt auth.
MacLean L. D.: *See* Himal H. S. jt auth., Mzabi R. jt auth.
Macpherson A. I. S.: *See* Chamberlain J. jt auth.
Mair W. S. J.: *See* Hill G. L. jt auth.
Malhotra V. J.: *See* Millar R. jt auth.
Malignancy, thyroid, pathology of, 757
Malignant ascites, resistant, treatment of, by insertion of peritoneo-atrial Holter valve, 104
  tumours of thyroid gland, aetiology and diagnosis of, 760
Mammary carcinoma, otherwise apparently 'early', significance of occult skeletal metastases, detected by skeletal scintigraphy, in patients with, 694
Man, observations of gastric mucosal blood flow using ^{99}Tc^{m} in rat and, 788
Manders J. T.: *See* Brock, Lord jt auth.
Mandible, occult osteomatous changes in, in patients with familial polyposis coli, 45
Marks C. G. and Ritchie J. K.: The complications of synchronous combined excision for adenocarcinoma of the rectum at St Mark's Hospital, 901
Marks J. E.: *See* Moossa A. R. jt auth.
Martinson J.: *See* Heimann P. jt auth.
Masks, surgical, of varying design and composition, efficiency of, 936

Master S. P.: *See* Carswell J. W. jt auth.
Matheson N. A. and Irving A. D.: Single layer anastomosis after rectosigmoid resection, 239
Mathur P. N.: *See* Pendse A. K. jt auth.
Maurice-Williams R. S. and Lucey J. J.: Raised intracranial pressure due to spinal tumours: 3 rare cases with a probable common mechanism, 92
M'Bamali E. I.: Results of modified Robert Jones operation for clawed hallux, 647
Meckel's diverticulum, bleeding, diagnosed by mesenteric arteriography, 882
Medullary carcinoma, inherited, of thyroid and phaeochromocytoma, report of family with, 264
Melanoma, place of frozen section in practical management of, 840
Melville-Jones C.: *See* Henderson W. J. jt auth.
Men with carcinoma of breast, survival rate of, 963
Meniscectomy, clinical features of degenerate meniscus with results of, 977
[illegible]cus, degenerate, clinical features of, with results of meniscectomy, 977
Menzies-Gow N.: *See* Bolton J. P. jt auth.
Mersilene mesh, hanging bladder stone formed around, 413
Mesenteric arteriography, bleeding Meckel's diverticulum diagnosed by, 882
Mesothelioma, peritoneal, 576
Metastases, occult skeletal, significance of, detected by skeletal scintigraphy, in patients with otherwise apparently 'early' mammary carcinoma, 694
Metcalfe-Gibson C.: A case of haemorrhage from volvulus of the gastric fundus, 224
Methylene blue infusion, parathyroid identification by, 747
Michie W.: Whither thyrotoxicosis? 673
de Miguel J.: Recurrence of gastric ulcer after selective vagotomy and pyloroplasty for chronic uncomplicated gastric ulcer: a 5–10-year follow-up, 875
Millar R., Rutherford W. H., Johnston S. and Malhotra V. J.: Injuries caused by rubber bullets: a report on 90 patients, 480
Miller S. S.: Abdominal approach for the ligation of bleeding oesophageal varices, 108
Millis R. R. and Thynne G. S. J.: *In situ* intraduct carcinoma of the breast: a long term follow-up, 957
Mishra O. P.: *See* Parekh B. R. jt auth.
Moossa A. R., Ree P. C., Marks J. E., Levin B., Platz C. E. and Skinner D. B.: Factors influencing local recurrence after abdominoperineal resection for cancer of the rectum and rectosigmoid, 727
Moossa A. R.: *See also* Helsby R. jt auth.
Morgan O. S., Nicholson G. D., Johnson P. S. and Atkinson D. W.: Xanthogranulomatous pyelonephritis: a report of 2 cases, 563
Morrice J. J.: *See* Sokhi G. S. jt auth.
Mosavy S. H.: *See* Hakami M. jt auth.
Motility changes in antrum after proximal gastric vagotomy, 215
Mott D.: *See* Schraibman I. G. jt auth.
Mouzas G. L. and Yeadon A.: Does the choice of suture material affect the incidence of wound infection? 952
Mucosal blood flow, gastric, observations of, using $^{99}\mathrm{Tc}^{\mathrm{m}}$ in rat and man, 788
Muller H.: True recurrence of hyperparathyroidism: proposed criteria of recurrence, 556
Murray W. R. and Bedi B. S.: The surgical management of ingrowing toenail, 409
Mzabi R., Himal H. S. and MacLean L. D.: Gas gangrene of the extremity: the presenting clinical picture in perforating carcinoma of the caecum, 373

Nakamuri T.: *See* Utsunomiya J. jt auth.
Naylor G. P.: *See* Schraibman I. G. jt auth.
Necrotizing pancreatitis, haemorrhagic and, 169
Negus D.: *See* Rickford C. R. K. jt auth.
Neoplastic change in duplications of alimentary tract, 269
Nephrectomy, *en bloc*, incision for, 565
Nerve, facial, injury of, during surgery of parotid gland, 401
Newborn, experimental studies on pathophysiological responses of, to injury, 868
Nicholson G. D.: *See* Morgan O. S. jt auth.
Nicol R.: *See* Blamey R. W. jt auth.
Nitrogen mustard as adjunctive chemotherapy for breast carcinoma, 497
Noble J.: Clinical features of the degenerate meniscus with the results of meniscectomy, 977
Nodular fasciitis: unusual cause of extradural spinal cord compression, 573
Nodules, cystic thyroid, 205
Norton L. W., Sweeney M. and Eiseman B.: Incidental appendicectomy with laparotomy for trauma, 487
Nowak K.: *See* Siddons H. jt auth.
Noxytiolin, effect of, in experimental peritonitis, 645
Nutritional support in management of external fistulas of alimentary tract, 100

Oates G. D.: *See* Keighley M. R. B. jt auth.
Obituary
  Vincent Zachary Cope, 668
O'Briain S.: *See* Clancy M. T. jt auth.
Obstruction, extrinsic duodenal, in infants and children, 125
  ureteric, due to sigmoid diverticulitis, 247
Occlusive arterial disease of lower limb, relationship between ultrasound assessment and angiography in, 64
Occult skeletal metastases, significance of, detected by skeletal scintigraphy, in patients with otherwise apparently 'early' mammary carcinoma, 694
O'Connor J.: *See* Young S. jt auth.
Oesophageal carcinoma, oesophagogastrostomy without drainage procedure in, 601
  sphincter, lower, response of, to maximal doses of pentagastrin, 11
  sphincter pressure, lower, after meals, relationship between changes in plasma gastrin and, 15
  stricture, peptic, management of, 448
  varices, bleeding, abdominal approach for ligation of, 108
Oesophagitis, peptic, with stricture, antrectomy with Roux-en-Y anastomosis in treatment of, 605
Oesophagogastrostomy without drainage procedure in oesophageal carcinoma, 601
Oesophagus, early management of corrosive burns of, 444
O'Keane M. A.: *See* Mackenzie R. J. jt auth.
Ong G. B. and Lee N. W.: Hepatic resection, 421
Ong G. B.: *See also* Ma M. K. G. jt auth.
Onuigbo W. I. B.: Tuberculous peripheral lymphadenitis in the Igbos of Nigeria, 323
Operating room and intensive care ward, importance of environmental conditions, especially temperature, in, 252
  theatre, environmental tests of linear flow ventilation for, 462
Operative biopsy of pancreas, 280
  cholangiography: reappraisal based on review of 400 cholangiograms, 166
Orr M. M. and Edwards A. J.: Neoplastic change in duplications of the alimentary tract, 269
Orthotopic liver transplantation: experimental study on prevention of infections with Gram-negative organisms, 513
  liver transplantation utilizing vascular stapling instrument, 438
Ossification in extradural fat in Paget's disease of spine, 571
Osteomatous changes, occult, in mandible in patients with familial polyposis coli, 45
Osteophytes, spinal, intra-abdominal symptoms arising from, 320
Owens, C. J.: *See* McCall I. W. jt auth.
Oxygen therapy, prolonged symptomatic and radiological remission of colonic gas cysts after, 837

Pacemakers, surgical complications of implanting, 929
Pacing, heart, surgical management and problems of, 186
Page R. E., Williams R. E. and Benson E. A.: Primary gastric tuberculosis: a case report, 618
Paget's disease of spine, ossification in extradural fat in, 571
Palmer M. K.: *See* Charlesworth D. jt auth.
Pancreas, operative biopsy of, 280
  and periampullary region, carcinoma of: clinical study in district general hospital, 130
Pancreatic pseudocysts in children: 4 cases from Uganda, 360
  pseudocysts, natural and unnatural history of, 37
  secretion of pig, exocrine, effect of acute ethanol administration on, 707
Pancreatitis, acute, aetiology of hypocalcaemia in, 115
  acute, prospective study of, 490
  chronic relapsing, recurrent pleural effusion in, 560
  haemorrhagic and necrotizing, 169
Pandit P. N.: *See* Prakash A. T. M. jt auth.
Papalexandris N.: *See* Vallidis E. jt auth.
Parathyroid(s) adenomas, localization of, by computer-assisted parathyroid scanning, 553
  arteriographic exposition of, 96
  identification by methylene blue infusion, 747
  origin, possible, of gastrin in patient with multiple endocrine adenopathy type 1, 313
  scanning, computer-assisted, localization of parathyroid adenomas by, 553
Pardy B. J. and Dudley H. A. F.: The effect of heparin and of acid-citrate-dextrose solution on screen filtration pressure of blood in experimental hypotension, 713
Parekh B. R., Reinboth G. and Mishra O. P.: Abdominoscrotal hydrocele, 629
Parenteral prophylactic gentamicin therapy, controlled trial of, in biliary surgery, 275
Parker R. W. and Shaw R. E.: Analgesic abuse in urologic practice, 298
Parnis R.: Gumma of the liver, 236
Parotid duct strictures, bilateral idiopathic, 468
  gland, injury of facial nerve during surgery of, 401
Pasupathy N. K.: *See* Gupta S. D. jt auth.
Pathophysiological responses of newborn to injury, experimental studies on, 868
Peacock J. H.: *See* Windle R. jt auth.
Pendse A. K., Mathur, P. N., Sharma M. M. and Gupta O. P.: Splenic-gonadal fusion, 624
Penis, secondary involvement of, by rectal cancer, 77
Pentagastrin, response of lower oesophageal spincter to maximal doses of, 11
Peptic oesophageal stricture, management of, 448
  oesophagitis with stricture, antrectomy with Roux-en-Y anastomosis in treatment of, 605
  ulcer, gastric mucosal resection in treatment of: 1–10 year clinical follow-up, 608
Perera A. B. V.: *See* Rasaretnam R. jt auth.
Perforated appendicitis with peritonitis, rabbit model of, 642
Perforating carcinoma of caecum, presenting clinical picture in: gas gangrene of extremity, 373
Periampullary region, carcinoma of pancreas and: clinical study in district general hospital, 130
Perineal wound management, controlled trial of three different methods of, following excision of rectum, 287
Peripheral lymphadenitis, tuberculous, in Igbos of Nigeria, 323
Peripheral venous pressure, some observations on, using non-invasive technique: preliminary report, 259
Peritoneal lavage, appraisal of, in diagnosis of acute abdomen, 119
  mesothelioma, 576
Peritoneo-atrial Holter valve, treatment of resistant malignant ascites by insertion of, 104
Peritonitis, experimental, effect of noxytiolin in, 645
  rabbit model of perforated appendicitis with, 642
Perry R. H.: *See* Sengupta R. P. jt auth.
Phaeochromocytoma, report of family with inherited medullary carcinoma of thyroid and, 264
Phenol injection, pilonidal sinus treated by, 407
  sympathectomy in treatment of intermittent claudication: controlled clinical trial, 68
Pig(s), construction of skin-lined hemithorax in, 351
  effect of acute ethanol administration on exocrine pancreatic secretion of, 707
  unimmunosuppressed, renal transplantation in: abnormal response, 474
Pigott H. and Ellis H.: Chronic hydradenitis suppurativa: a report of 9 cases, 394
Pilonidal sinus treated by phenol injection, 407
Plasma catecholamines in severely injured patients: prospective study on 45 patients with multiple injuries, 177
  gastrin, and lower oesophageal sphincter pressure after meals, relationship between changes in, 15
Platz C. E.: *See* Moossa A. R. jt auth.
Plethysmography, impedance and strain gauge, comparison of, in measurement of blood flow in lower limb, 909
Pleural effusion, recurrent, in chronic relapsing pancreatitis, 560
Pneumatic bandaging technique, elastic bandaging, Puddifoot dressing and, compared: pressure measurements beneath below-knee amputation stump bandages, 982
Pneumatosis cystoides intestinalis with unexplained ascites in Ethiopian patients, 379
Polak J. M.: *See* Cassar J. jt auth.
Pollock A. V.: The treatment of resistant malignant ascites by insertion of a peritoneo-atrial Holter valve, 104
Pollock A. V. and Evans M.: Povidone-iodine for the control of surgical wound infection: a controlled clinical trial against topical cephaloridine, 292
Pollock A. V.: *See also* Evans C. jt auth.
Polyposis coli, epidermoid cysts, and Gardner's syndrome, 387
  coli, occult osteomatous changes in mandible in patients with, 45
Popescu D. T.: *See* Schalm S. W. jt auth.
Popliteal arterial thromboses, complete disappearance of, in 2 patients, 141
Portocaval anastomosis, prognosis after: 15-year follow-up, 701
Postoperative deep vein thrombosis, early detection of: assessment of Doppler ultrasound, physical examination and temperature chart, 182
  problems and management after hepatic resection for blunt injury to liver, 189
Postvagotomy diarrhoea, cause and treatment of, 309
  dysphagia, 354
Potassium, effect of raising concentration of, in blood or intestinal lumen on transport of potassium in dog intestine, 455
  total body, total body water, total exchangeable sodium and, long term changes in, before and after ileostomy, 524
Povidone-iodine for control of surgical wound infection: controlled clinical trial against topical cephaloridine, 292
  prophylactic interparietal, in abdominal surgery, 792
Powell D. J.: *See* Robin P. E. jt auth.
Prakash A. T. M., Sharma L. K. and Pandit P. N.: Primary carcinoma of the gallbladder, 33
Pre-gangrene of lower limb, clinical trial of method of treatment for: intra-arterial infusion of Solcoseryl, 337
Pregnancy, early, general anaesthesia during, 471
Prophylactic gentamicin therapy, parenteral, controlled trial of, in biliary surgery, 275
Prosthesis, upper limb, immediate operative fitting of, at time of amputation, 634
Proximal gastric vagotomy, motility changes in antrum after, 215
Prudhoe K.: *See* Gill G. V. jt auth.

Pseudocysts, pancreatic, in children: 4 cases from Uganda, 360
  pancreatic, natural and unnatural history of, 37
Puddifoot dressing, elastic bandaging and pneumatic bandaging technique compared: pressure measurements beneath below-knee amputation stump bandages, 982
Pullan B. R.: *See* Taylor T. V. jt auth.
Pyelonephritis, xanthogranulomatous: report of 2 cases, 563
Pyloroplasty, recurrence of gastric ulcer after selective vagotomy and, for chronic uncomplicated gastric ulcer: 5–10 year follow-up, 875
Pylorus, innervated and intact antrum and, importance of, in preventing postoperative duodenogastric reflux and gastritis, 845

Quadriceps tendons, bilateral simultaneous rupture of, 918
Quesnel L. B.: The efficiency of surgical masks of varying design and composition, 936
Quin R. O.: *See* Fyfe T. jt auth.
Quoraishi A. H.: *See* Keighley M. R. B. jt auth.

Rabbit model of perforated appendicitis with peritonitis, 642
Radio-isotope hepatogram, value of, in jaundiced patient, 781
Raine P. A. M. and Gunn A. A.: Acute cholecystitis, 697
Rajendraprasad G. B.: *See* Subrahmanian M. V. jt auth.
Ramani P. S., Kalbag R. M. and Sengupta R. P.: Cervical spinal interbody fusion with Kiel bone, 147
Rao B. D.: *See* Subrahmanian M. V. jt auth.
Rasaretnam R., Perera A. B. V. and Kumarasinghe M.: Recurrent pleural effusion in chronic relapsing pancreatitis, 560
Rasaretnam R.: *See also* Thavendran A. jt auth.
Rashid A.: *See* Evans C. jt auth.
Rat and man, observations of gastric mucosal blood flow using $^{99}\mathrm{Tc}^{m}$ in, 788
Rawat S. S., Jain G. K. and Gupta H. K. D.: Intra-abdominal symptoms arising from spinal osteophytes, 320
Reconstruction, aorto-iliac, with special reference to extraperitoneal approach, 596
Rectal cancer, secondary involvement of penis by, 77
Rectosigmoid, factors influencing local recurrence after abdominoperineal resection for cancer of rectum and, 727
  resection, single layer anastomosis after, 239
Rectum, complications of synchronous combined excision for adenocarcinoma of, at St Mark's Hospital, 901
  controlled trial of three different methods of perineal wound management following excision of, 287
  and rectosigmoid, factors influencing local recurrence after abdominoperineal resection for cancer of, 727
Recurrences, suspected, of cancer of stomach, is 'second look surgery' justified in? 226
Ree P. C.: *See* Moossa A. R. jt auth.
Rees B. I.: Secondary involvement of the penis by rectal cancer, 77
Rees B. I. and Bolton P. M.: Ureteric obstruction due to sigmoid diverticulitis, 247
Reflux, postoperative duodenogastric, and gastritis, importance of innervated and intact antrum and pylorus in preventing, 845
Reid D. R. K. and Rogers I. M.: The negative cholecystogram in gallbladder disease, 581
Reid D. R. K., Rogers I. M. and Calder J. F.: The cholecystokinin test: an assessment, 317
Reinboth G.: *See* Parekh B. R. jt auth.
Renal transplantation, gastric acid secretion following, 737
  transplantation in unimmunosuppressed pig: abnormal response, 474
Resection, hepatic, postoperative problems and management after, for blunt injury to liver, 189
  rectosigmoid, single layer anastomosis after, 239
Reservoir ileostomies, 26, experience with, 893

Reviews (Titles):
  Abdominal echography. Ultrasound in the diagnosis of abdominal conditions (E. Barnett and P. Morley), 501
  Abdominal operations. Volumes 1 *and* 2 (ed. R. Maingot), 989
  Accident surgery and orthopaedics for students (J. R. Pearson and R. T. Austin), 251
  Acupuncture for physicians (T. Matsumoto), 586
  Advances in cardiovascular surgery (ed. J. W. Kirklin), 587
  Advances in surgery. Volume 7, 1973 (ed. J. D. Hardy and R. M. Zollinger), 333
  Aims and motives in clinical medicine. A practical approach to medical ethics (B. P. Bliss and A. G. Johnson), 927
  Alexis Carrel. Visionary surgeon (W. S. Edwards and P. D. Edwards), 672
  The arteries and veins of the human spinal cord from birth (G. F. Dommisse), 987
  Arthroplasty of the hip (ed. G. Chapchal), 334
  Atlas of the battered child syndrome (J. M. Cameron and I. J. Rae), 987
  Atlas of hand surgery (R. A. Chase), 417
  Atlas of human anatomy. Volumes 1, 2 *and* 3 (ed. F. H. T. Figge and W. J. Hild), 501
  Atlas of orthopaedic surgery. Volumes 1 *and* 2 (L. A. Goldstein and C. Dickerson), 756
  Atlas of vascular surgery (R. R. Linton), 585
  Basic clinical surgery for nurses and medical students (ed. J. McFarland), 81
  Basic gastro-enterology (J. M. Naish and A. E. Read), 335
  Biochemical values in clinical medicine (R. D. Eastham), 987
  Blood compatible synthetic polymers (S. D. Bruck), 166
  Bonney's gynaecological surgery (ed. J. Howkings and Sir John Stallworthy), 415
  Bronchial carcinoma (T. W. Shields and R. E. Ritts), 588
  Cancer handbook of epidemiology and prognosis (J. A. H. Waterhouse), 168
  Cardiac arrest and resuscitation (H. E. Stephenson), 756
  Cardiovascular applications of ultrasound (ed. R. S. Reneman), 585
  Care of the ostomy patient (V. C. Vukovich and R. D. Grubb), 83
  Central rhythmic and regulation: circulation, respiration, extrapyramidal motor system (ed. W. Umbach and H. P. Koepchen), 167
  The cervical spine (R. W. Bailey), 251
  Children's fractures (M. Rang), 670
  China medicine as we saw it (ed. J. R. Quinn), 987
  Chirurgie (P. A. A. Klok), 584
  Chirurgie der Gegenwart (ed. R. Zenker, F. Deucher and W. Schink), 83, 335, 416, 502
  Clinical anesthesia, monitoring in anesthesia, volume 9, *numbers* 2 *and* 3 (ed. W. H. L. Dornette), 333
  Clinical cardiac radiology (K. Jefferson and S. Rees), 165
  Clinical embryology for medical students (R. S. Snell), 988
  Clinical neuro-surgery (Congress of Neurological Surgeons), 416
  Concise anatomy (M. E. Todd and G. M. Wyburn), 927
  A concise surgery of the acute abdomen (J. A. Shepherd), 925
  Corticosteroid and ACTH treatment. Principles and problems (A. B. Myles and J. R. Daly), 502
  Cryosurgery in urology: international symposium in Stuttgart, 1973 (ed. H. J. Reuter), 586
  Current medical diagnosis and treatment (M. A. Krupp and M. J. Chatton), 335
  Current pediatric diagnosis and treatment (H. Kempe, H. K. Silver, D. O'Brien and associate authors), 503
  Current practice in orthopaedic surgery. Volume 5, 1973 (ed. J. P. Ahstrom jun.), 82
  The cutting edge. Early history of the surgeons of London (R. T. Beck), 420

Reviews (Titles), *continued*
- *Diagnosis and early management of trauma emergencies. A manual for the emergency service* (ed. R. J. Touloukian and T. J. Krizek), 416
- *Die vaginalen Operationen* (G. Reiffenstuhl and W. Platzer), 336
- *Digestive surgery. Proceedings of the Second World Congress of Collegium Internationale Chirurgiae Digestivae* (ed. L. F. Hollender and G. D'Onofrio), 989
- *Diseases of the ear* (S. R. Mawson), 503
- *Diseases of the knee joint* (I. S. Smillie), 336
- *The doctor's lawyer. A legal handbook for doctors* (M. J. Lane), 335
- *The ductus arteriosus* (D. E. Cassels), 165
- *Dupuytren's disease* (ed. J. T. Hueston and R. Tubiana), 418
- *Emergency abdominal surgery, in infancy, childhood and adult life* (P. F. Jones), 417
- *Emergency anaesthesia* (ed. H. L. Thornton), 927
- *Endoscopy of the small intestine with retrograde pancreatocholangiography* (ed. L. Demling and M. Classen), 501
- *The esophagus* (ed. W. S. Payne and A. M. Olsen), 334
- *Essentials of urology* (D. E. Sturdy), 335
- *The etiology of human breast cancer* (A. N. Papaioannou), 988
- *The Faber medical dictionary* (ed. Sir Cecil Wakeley, now revised by J. G. Bate), 753
- *Ferguson's surgery of the ambulatory patient* (ed. M. W. Wolcott), 754
- *Fibre-optic endoscopy* (P. R. Salmon), 753
- *Flexible implant resection arthroplasty in the hand and extremities* (A. B. Swanson), 586
- *Fluid, electrolyte and nutrient therapy in surgery* (E. E. Mason), 419
- *Functional anatomy of the digestive system* (R. M. H. McMinn and M. H. Hobdell), 501
- *Fundamentals of colon surgery* (L. W. Ottinger), 926
- *Gastro-entero-pancreatic endocrine system. A cell-biological approach* (ed. T. Fujita), 333
- *Gastrointestinal pan-endoscopy* (L. H. Berry and international contributors), 926
- *General opthalmology* (D. Vaughan and T. Asbury), 502
- *General pathology. A programmed text* (ed. T. H. Kent), 925
- *The genetics of locomotive disorders* (C. O. Carter and T. J. Fairbank), 420
- *Grundlagen der Nachsorge nach chirurgischen und urologischen Eingriffen* (G. Jorns, W. Remde and H. Gerhard), 80
- *A guide to disaster management based on proceedings of an inter-service conference held in the Walton Conference Centre, The Southern General Hospital, Glasgow, in September* 1973, *and a report on disaster response in America and Canada following the tornadoes of April* 1974 (ed. W. Sillar), 671
- *Hair transplant surgery* (O'T. T. Norwood), 584
- *Handbook of obstetrics and gynaecology* (R. C. Benson), 753
- *Handbook of orthoptic principles* (G. T. W. Cashell and I. M. Durran), 587
- *Handbook of psychiatry* (ed. P. Solomon and V. D. Patch), 418
- *A history of the Army Medical Department. Volumes* 1 *and* 2 (Lt-Gen. Sir Neil Cantlie), 83
- *Immunological aspects of transplantation surgery* (ed. R. Calne), 166
- *Instructional course lectures. Volume XXII*, 1973 (The American Academy of Orthopaedic Surgeons), 251
- *Instructional course lectures. Volume XXIII*, 1974 (The American Academy of Orthopaedic Surgeons), 927
- *Klinische Urologie. Ein Lehrbuch* (ed. C. E. Aiken and W. Staehler), 83
- *Larrey: surgeon to Napoleon's Imperial Guard* (R. G. Richardson), 168

Reviews (Titles), *continued*
- *Lectures on methodology of clinical research* (M. Hamilton), 80
- *Lessons of leucotomy* (ed. A. Robin and D. Macdonald), 989
- *The liver and its diseases* (F. Schaffner, S. Sherlock and C. M. Leevy), 584
- *Lymphography—clinical and experimental* (ed. B. W. M. Gooneratne), 587
- *Machine diagnosis and information retrieval in medicine in the USSR* (ed. A. A. Vischnevskiy, I. I. Artobolevskiy and M. L. Bykhovskiy), 251
- *Mammary cancer and neuroendocrine therapy* (ed. B. A. Stoll), 250
- *The management of trauma* (ed. W. F. Ballinger, R. B. Rutherford and G. D. Zuidema), 81
- *A manual of head injuries in general surgery* (G. Martin), 588
- *Medical and surgical emergencies* (ed. J. H. Schneewind), 586
- *Microbes and man. A laboratory manual for students in the health sciences* (I. J. Barnes, H. W. Seeley jun. and P. J. Van Denmark), 587
- *Modern trends in paediatrics*—4 (ed. J. Apley), 502
- *The myocardium: failure and infarction* (ed. E. Braunwald), 417
- *Needle biopsy* (T. J. Deeley), 167
- *Nontoxic goiter. Concept and controversy* (J. I. Hamburger), 80
- *Operating theatre technique* (R. J. Brigden), 333
- *Orthopaedic surgery* (E. L. Compere), 415
- *Orthopaedic surgery and traumatology* (ed. R. De Marneffe and E. Vander), 82
- *Pädiatrische Intensivbehandlung* (V. von Loewenich and H. Koch), 333
- *Pathology of the cardiomyopathies* (B. McKinney), 252
- *Pediatric orthopedic nursing* (N. E. Hilt and E. W. Schmitt), 989
- *The physiology of the joints. Volume* 3. *The trunk and the vertebral column* (I. A. Kapandji), 419
- *Postgraduate surgery lectures* 2 (ed. J. McFarland), 671
- *The practical management of head injuries* (J. M. Potter), 419
- *Practical surgical management* (A. M. C. Macgregor), 415
- *Principles and practice of modern surgery* (A. L. Som), 250
- *Progress in paediatric neurosurgery* (ed. K. A. Bushe, O. Spoerri and J. Shaw), 250
- *Progress in pediatric surgery. Volume* 7 (ed. P. P. Rickham, W. Ch. Hecker and J. Prevot), 250
- *Prostheses and rehabilitation after arm amputation* (L. F. Bender), 754
- *Quick reference to surgical emergencies* (ed. G. W. Shaftan and B. Gardner), 587
- *Radiology of bone diseases* (G. B. Greenfield), 988
- *The radiology of emergency medicine* (J. H. Harris and W. H. Harris), 925
- *Reactions to injury and burns and their clinical importance* (S. Sevitt), 755
- *Recent advances in thrombosis* (ed. L. Poller), 82
- *Renal histopathology. A light microscopy study of renal disease* (R. Meadows), 81
- *Retinal detachment. The essentials of management* (H. B. Chawla), 80
- *Review of medical microbiology* (E. Jawetz, J. L. Melnick and E. A. Adelberg), 334
- *Review of medical pharmacology* (F. H. Meyers, E. Jawetz and A. Goldfien), 420
- *Roentgen examinations in acute abdominal diseases* (J. Friemann-Dahl), 585
- *Rontgenuntersuchung der Brust. Technik Diagnostik Differentialdiagnose Ergebnisse* (W. Hoeffken and M. Lanyi), 81
- *Safe central venous nutrition. Guidelines for prevention and management of complications* (M. H. Parsa, J. M. Ferrer and D. V. Habif), 502

Reviews (Titles), *continued*
Scientific foundations of surgery (ed. C. Wells, J. Kyle and J. E. Dunphy), 335
Sémiologie chirurgicale (L. Léger), 671
Soviet research in pharmacology and toxicology (W. H. Fitzpatrick), 672
Spinal deformity in neurological and muscular disorders (ed. J. H. Hardy), 926
The spleen (A. I. S. Macpherson, J. Richmond and A. E. Stuart), 166
Stress fractures (M. Devas), 988
Stroke. Diagnosis and management. Current procedures and equipment (ed. W. S. Fields and J. Moossy), 168
The structure and biochemistry of cartilage (A. Serafini-Fracassini and J. W. Smith), 168
Surgery (R. M. Kirk, J. Maynard and A. N. Henry), 334
1972 *Surgery annual. Volume* 4 (ed. P. Cooper and L. M. Nyhus), 83
Surgery annual: 1974 *Vol. VI* (ed. L. M. Nyhus), 755
The surgery of the central nervous system (D. W. C. Northfield), 82
Surgery of the gastrointestinal tract (ed. J. S. Najarian and J. P. Delaney), 250
Surgery of the liver and portal circulation (W. V. McDermott), 334
Surgery of the lung. The Coventry conference (ed. R. E. Smith and W. G. Williams), 252
Surgical aspects of haemodialysis (P. R. F. Bell and K. C. Calman), 584
Surgical forum—the liver (ed. R. Smith), 754
Surgical pathology (L. V. Ackerman and J. Rosai), 418
Surgical technology. Basis for clinical practice (M. L. Hoeller), 585
Surgical treatment of facial injuries (V. H. Kazanjian and J. M. Converse), 418
Surgical treatment of head and neck tumours (ed. J. F. Barbosa), 503
Symposium on management of cleft lip and palate and associated deformities. Volume 8 (ed. N. G. Georgiade), 756
Symposium on reconstructive hand surgery. Volume 9 (ed. J. W. Littler, L. M. Cramer and J. W. Smith), 588
A synopsis of anaesthesia (J. A. Lee and R. S. Atkinson), 166
The systematic manifestations of inflammatory bowel disease (ed. W. M. Lukash and R. B. Johnson), 755
A textbook of surgery (ed. Mahadevan), 670
Therapeutic aspects of nutrition (ed. J. H. P. Jonxis, H. K. A. Visser and J. A. Troelstra), 80
Transfusion of blood preserved by freezing (S. Sumida), 415
Trauma management (E. F. Cave, J. F. Burke and R. J. Boyd), 671
The treatment of breast cancer (ed. Sir Hedley Atkins), 416
The treatment of chronic pain (ed. F. D. Hart), 167
The treatment of prostatic hypertrophy and neoplasia (ed. J. E. Castro), 420
Tumour surgery of the head and neck (R. S. Pollack), 925
Tumours of the esophagus and stomach (S-C. Ming), 503
Tumours of the extra-adrenal paraganglion system (including chemoreceptors) (G. G. Glenner and P. M. Grimley), 82
Tumours of the major salivary glands (atlas of tumour pathology, second series) (A. C. Thackray and R. B. Lucas), 671
Tumours of the male genital system (F. K. Mostofi and E. B. Price), 165
Urology and renal medicine (J. E. Newsam and J. J. B. Petrie), 925
Vagotomy. Latest advances (ed. F. Holle and S. Andersson), 926
Vascular malformations (angiodysplasia) (ed. E. Malan), 417

Reviews (Titles), *continued*
Vascular surgery. Volume I. Peripheral arterial diseases (J. J. Cranley), 584
Ventilatory and phonatory control systems (ed. B. Wyke), 755
1974 *Year book of plastic and reconstructive surgery* (ed. K. L. Stephenson et al.), 419
1974 *Year book of surgery* (ed. S. I. Schwartz et al.), 753

Reviews (Authors):
Ackerman L. V. and Rosai J.: *Surgical pathology*, 418
Adelberg E. A.: *See* Jawetz E. jt auth.
Ahstrom J. P. jun.: *Current practice in orthopaedic surgery. Volume* 5, 1973 (ed.), 82
Alken C. E. and Staehler W.: *Klinische Urologie. Ein Lehrbuch* (ed.), 83
The American Academy of Orthopaedic Surgeons: *Instructional course lectures. Volume XXII*, 1973, 251
The American Academy of Orthopaedic Surgeons: *Instructional course lectures. Volume XXIII*, 1974, 927
Andersson A.: *See* Holle F. jt auth.
Apley J.: *Modern trends in paediatrics*—4 (ed.), 502
Artobolevskiy I. I.: *See* Vischnevskiy A. A. jt ed.
Asbury T.: *See* Vaughan D. jt auth.
Atkins Sir Hedley: *The treatment of breast cancer* (ed.), 416
Atkinson R. S.: *See* Lee J. A. jt auth.
Austin R. T.: *See* Pearson J. R. jt auth.
Bailey R. W.: *The cervical spine*, 251
Ballinger W. F., Rutherford R. B. and Zuidema G. D.: *The management of trauma* (ed.), 81
Barbosa J. F.: *Surgical treatment of head and neck tumours*, 503
Barnes I. J., Seeley H. W. jun. and Van Denmark P. J.: *Microbes and man. A laboratory manual for students in the health sciences*, 587
Barnett E. and Morley P.: *Abdominal echography. Ultrasound in the diagnosis of abdominal conditions*, 501
Bate J. G.: *See* Wakeley Sir Cecil jt ed.
Beck R. T.: *The cutting edge. Early history of the surgeons of London*, 420
Bell P. R. F. and Calman K. C.: *Surgical aspects of haemodialysis*, 584
Bender L. F.: *Prostheses and rehabilitation after arm amputation*, 754
Benson R. C.: *Handbook of obstetrics and gynaecology*, 753
Berry L. H.: *Gastrointestinal pan-endoscopy*, 926
Bliss B. P. and Johnson A. G.: *Aims and motives in clinical medicine. A practical approach to medical ethics*, 927
Boyd R. J.: *See* Cave E. F. jt auth.
Braumwald E.: *The myocardium: failure and infarction* (ed.), 417
Brigden R. J.: *Operating theatre techniques*, 333
Bruck S. D.: *Blood compatible synthetic polymers*, 166
Burke J. F.: *See* Cave E. F. jt auth.
Bushe K. A., Spoerri O, and Shaw J.: *Progress in paediatric neurosurgery* (ed.), 250
Bykhovskiy M. L.: *See* Vischnevskiy A. A. jt ed.
Calman K. C.: *See* Bell P. R. F. jt auth.
Calne R.: *Immunological aspects of transplantation surgery* (ed.), 166
Cameron J. M. and Rae L. J.: *Atlas of the battered child syndrome*, 987
Cantlie Lt-Gen. Sir Neil: *A history of the Army Medical Department. Volumes* 1 *and* 2, 83
Carter C. O. and Fairbank T. J.: *The genetics of locomotive disorders*, 420
Cashell G. T. W. and Durran I. M.: *Handbook of orthoptic principles*, 587
Cassels D. E.: *The ductus arteriosus*, 165
Castro J. E.: *The treatment of prostatic hypertrophy and neoplasia* (ed.), 420

Reviews (Authors), *continued*
Cave E. F., Burke J. F. and Boyd R. J.: *Trauma management*, 671
Chapchal G.: *Arthroplasty of the hip* (ed.), 334
Chase R. A.: *Atlas of hand surgery*, 417
Chatton M. J.: *See* Krupp M. A. jt auth.
Chawla H. B.: *Retinal detachment. The essentials of management*, 80
Classen M.: *See* Demling L. jt ed.
Compere E. L.: *Orthopaedic surgery*, 415
Congress of Neurological Surgeons: *Clinical neurosurgery*, 416
Converse J. M.: *See* Kazanjian V. H. jt auth.
Cooper P. and Nyhus L. M.: 1972 *Surgery annual. Volume* 4 (ed.), 83
Cramer L. M.: *See* Littler J. W. jt ed.
Cranley J. J.: *Vascular surgery. Volume I. Peripheral arterial diseases*, 584
Daly J. B.: *See* Myles A. B. jt auth.
Deeley T. J.: *Needle biopsy*, 167
Delaney J. P.: *See* Najarian J. S. jt ed.
Demling L. and Classen M.: *Endoscopy of the small intestine with retrograde pancreatocholangiography* (ed.), 501
Deucher F.: *See* Zenker R. jt ed.
Devas M.: *Stress fractures*, 988
Dickerson C.: *See* Goldstein L. A. jt auth.
Dornette W. H. L.: *Clinical anesthesia, monitoring in anesthesia, volume* 9, *numbers* 2 *and* 3 (ed.), 333
Dunphy J. E.: *See* Wells C. jt ed.
Durran I. M.: *See* Cashell G. T. W. jt auth.
Eastham R. D.: *Biochemical values in clinical medicine*, 987
Edwards P. D.: *See* Edwards W. S. jt auth.
Edwards W. S. and Edwards P. D.: *Alexis Carrel. Visionary surgeon*, 672
Fairbank T. J.: *See* Carter C. O. jt auth.
Ferrer J. M.: *See* Parsa M. H. jt auth.
Fields W. S. and Moossy J.: *Stroke. Diagnosis and management. Current procedures and equipment* (ed.), 168
Figge F. H. T. and Hild W. J.: *Atlas of human anatomy. Volumes* 1, 2 *and* 3 (ed.), 501
Fitzpatrick W. H.: *Soviet research in pharmacology and toxicology*, 672
Friemann-Dahl J.: *Roentgen examinations in acute abdominal diseases*, 585
Fujita T.: *Gastro-entero-pancreatic endocrine system. A cell-biological approach* (ed.), 333
Gardner B.: *See* Shaftan G. W. jt ed.
Georgiade N. G.: *Symposium on management of cleft lip and palate and associated deformities. Volume* 8 (ed.), 756
Gerhard H.: *See* Jorns G. jt auth.
Glenner G. G. and Grimley P. M.: *Tumours of the extra-adrenal paraganglion system (including chemoreceptors)*, 82
Goldfien A.: *See* Meyers F. H. jt auth.
Goldstein L. A. and Dickerson C.: *Atlas of orthopaedic surgery. Volumes* 1 *and* 2, 756
Gooneratne B. W. M.: *Lymphography—clinical and experimental* (ed.), 587
Greenfield G. B.: *Radiology of bone diseases*, 988
Grimley P. M.: *See* Glenner G. G. jt auth.
Grubb R. D.: *See* Vukovich V. C. jt auth.
Habif D. V.: *See* Parsa M. H. jt auth.
Hamburger J. I.: *Nontoxic goiter. Concept and controversy*, 80
Hamilton M.: *Lectures on methodology of clinical research*, 80
Hardy J. D. and Zollinger R. M.: *Advances in surgery. Volume* 7, 1973 (ed.), 333
Hardy J. H.: *Spinal deformity in neurological and muscular disorders* (ed.), 926
Harris J. H. and Harris W. H.: *The radiology of emergency medicine*, 925
Harris W. H.: *See* Harris J. H. jt auth.

Reviews (Authors), *continued*
Hart F. D.: *The treatment of chronic pain* (ed.), 167
Henry A. M.: *See* Kirk R. M. jt auth.
Hild W. J.: *See* Figge F. H. T. jt ed.
Hilt N. E. and Schmitt E. W.: *Pediatric orthopedic nursing*, 989
Hobdell M. H.: *See* McMinn R. M. H. jt auth.
Hoeffken W. and Lanyi M.: *Rontgenuntersuchung der Brust. Technik Diagnostik Differentialdiagnose Ergebnisse*, 81
Hoeller M. L.: *Surgical technology. Basis for clinical practice*, 585
Holle F. and Andersson S.: *Vagotomy. Latest advances* (ed.), 926
Hollender L. F. and D'Onofrio G.: *Digestive surgery. Proceedings of the Second World Congress of Collegium Internationale Chirurgiae Digestivae* (ed.), 989
Howkings J. and Stallworthy Sir John: *Bonney's gynaecological surgery* (ed.), 415
Hueston J. T. and Tubiana R.: *Dupuytren's disease* (ed.), 418
Jawetz E., Melnick J. L. and Adelberg E. A.: *Review of medical microbiology*, 334
Jawetz E.: *See also* Meyers F. H. jt auth.
Jefferson K. and Rees S.: *Clinical cardiac radiology*, 165
Johnson R. B.: *See* Lukash W. M. jt ed.
Jones P. F.: *Emergency abdominal surgery, in infancy, childhood and adult life*, 417
Jonxis J. H. P., Visser H. K. A. and Troelstra J. A.: *Therapeutic aspects of nutrition* (ed.), 80
Jorns G., Remde W. and Gerhard H.: *Grundlagen der Nachsorge nach chirurgischen und urologischen Eingriffen*, 80
Kapandji I. A.: *The physiology of the joints. Volume* 3. *The trunk and the vertebral column*, 419
Kazanjian V. H. and Converse J. M.: *Surgical treatment of facial injuries*, 418
Kempe H., Silver H. K., O'Brien D. and associate authors: *Current pediatric diagnosis and treatment*, 503
Kent T. H.: *General pathology. A programmed text* (ed.), 925
Kirk R. M., Maynard J. and Henry A. N.: *Surgery*, 334
Kirklin J. W.: *Advances in cardiovascular surgery* (ed.), 587
Klok P. A. A.: *Chirurgie*, 584
Koch H.: *See* von Loewenich V. jt auth.
Koepchen H. P.: *See* Umbach W. jt ed.
Krizek T. J.: *See* Touloukian R. T. jt ed.
Krupp M. A. and Chatton M. J.: *Current medical diagnosis and treatment*, 335
Kyle J.: *See* Wells C. jt ed.
Lane M. J.: *The doctor's lawyer. A legal handbook for doctors*, 335
Lanyi M.: *See* Hoeffken W. jt auth.
Lee J. A. and Atkinson R. S.: *A synopsis of anaesthesia*, 166
Leevy C. M.: *See* Schaffner F. jt auth.
Léger L.: *Sémiologie chirurgicale*, 671
Linton R. R.: *Atlas of vascular surgery*, 585
Littler J. W., Cramer L. M. and Smith J. W.: *Symposium on reconstructive hand surgery. Volume* 9 (ed.), 588
von Loewenich V. and Koch H.: *Pädiatrische Intensivbehandlung*, 333
Lucas R. B.: *See* Thackray A. C. jt auth.
Lukash W. M. and Johnson R. B.: *The systematic manifestations of inflammatory bowel disease* (ed.), 755
McDermott W. V.: *Surgery of the liver and portal circulation*, 334
Macdonald D.: *See* Robin A. jt ed.
McFarland J.: *Basic clinical surgery for nurses and medical students* (ed.), 81
McFarland J.: *Postgraduate surgery lectures* 2 (ed.), 671
Macgregor A. M. C.: *Practical surgical management*, 415
McKinney B.: *Pathology of the cardiomyopathies*, 252

Reviews (Authors), *continued*
McMinn R. M. H. and Hobdell M. H.: *Functional anatomy of the digestive system*, 501
Macpherson A. I. S., Richmond J. and Stuart A. E.: *The spleen*, 166
Mahadevan: *A textbook of surgery*, 670
Maingot R.: *Abdominal operations. Volumes 1 and 2* (ed.), 989
Malan E.: *Vascular malformations (angiodysplasia)* (ed.), 417
De Marneffe R. and Vander E.: *Orthopaedic surgery and traumatology* (ed.), 82
Martin G.: *A manual of head injuries in general surgery*, 588
Mason E. E.: *Fluid, electrolyte and nutrient therapy in surgery*, 419
Matsumoto T.: *Acupuncture for physicians*, 586
Mawson S. R.: *Diseases of the ear*, 503
Maynard J.: *See* Kirk R. M. jt auth.
Meadows R.: *Renal histopathology. A light microscopy study of renal disease*, 81
Melnick J. L.: *See* Jawetz E. jt auth.
Meyers F. H., Jawetz E. and Goldfien A.: *Review of medical pharmacology*, 420
Ming S-C.: *Tumours of the esophagus and stomach*, 503
Moossy J.: *See* Fields W. S. jt ed.
Morley P.: *See* Barnett E. jt auth.
Mostafi F. K. and Price E. B.: *Tumours of the male genital system*, 165
Myles A. B. and Daly J. B.: *Corticosteroid and ACTH treatment. Principles and problems*, 502
Naish J. M. and Read A. E.: *Basic gastro-enterology*, 335
Najarian J. S. and Delaney J. P.: *Surgery of the gastro-intestinal tract* (ed.), 250
Newsam J. E. and Petrie J. J. B.: *Urology and renal medicine*, 925
Northfield D. W. C.: *The surgery of the central nervous system*, 82
Norwood O'T. T.: *Hair transplant surgery*, 584
Nyhus L. M.: *Surgery annual: 1974 Vol. VI* (ed.), 755
Nyhus L. M.: *See also* Cooper P. jt ed.
O'Brien D.: *See* Kempe H. jt auth.
Olsen A. M.: *See* Payne W. S. jt ed.
D'Onofrio G. D.: *See* Hollender L. F. jt ed.
Ottinger L. W.: *Fundamentals of colon surgery*, 926
Papaioannou A. N.: *The etiology of human breast cancer*, 988
Parsa M. H., Ferrer J. M. and Habif D. V.: *Safe central nutrition. Guidelines for prevention and management of complications*, 502
Patch V. D.: *See* Solomon P. jt ed.
Payne W. S. and Olsen A. M.: *The esophagus* (ed.), 334
Pearson J. R. and Austin R. T.: *Accident surgery and orthopaedics for students*, 251
Petrie J. J. B.: *See* Newsam J. E. jt auth.
Platzer W.: *See* Reiffenstuhl G. jt auth.
Pollack R. S.: *Tumour surgery of the head and neck*, 925
Poller L.: *Recent advances in thrombosis* (ed.), 82
Potter J. M.: *The practical management of head injuries*, 419
Prevot J.: *See* Rickham P. P. jt ed.
Price E. B.: *See* Mostafi F. K. jt auth.
Quinn J. R.: *China medicine as we saw it* (ed.), 987
Rae L. J.: *See* Cameron J. M. jt auth.
Rang M.: *Children's fractures*, 670
Read A. E.: *See* Naish J. M. jt auth.
Rees S.: *See* Jefferson K. jt auth.
Reiffenstuhl G. and Platzer W.: *Die vaginalen Operationen*, 336
Remde W.: *See* Jorns G. jt auth.
Reneman R. S.: *Cardiovascular applications of ultrasound* (ed.), 585
Reuter H. J.: *Cryosurgery in urology: international symposium in Stuttgart*, 1973, 586
Richardson R. G.: *Larrey: surgeon to Napoleon's Imperial Guard*, 168
Richmond J.: *See* Macpherson A. I. S. jt auth.

Reviews (Authors), *continued*
Rickham P. P., Hecker W. Ch. and Prevot J.: *Progress in pediatric surgery. Volume* 7 (ed.), 250
Ritts R. E.: *See* Shields T. W. jt auth.
Robin A. and Macdonald D.: *Lessons of leucotomy* (ed.), 989
Rosai J.: *See* Ackerman L. V. jt auth.
Rutherford R. B.: *See* Ballinger W. F. jt ed.
Salmon P. R.: *Fibre-optic endoscopy*, 753
Schaffner F., Sherlock S. and Leevy C. M.: *The liver and its diseases*, 584
Schink W.: *See* Zenker R. jt ed.
Schmitt E. W.: *See* Hilt N. E. jt auth.
Schneewind J. H.: *Medical and surgical emergencies* (ed.), 586
Schwartz S. L. et al.: 1974 *Year book of surgery* (ed.), 753
Seeley H. W. jun: *See* Barnes I. J. jt auth.
Serafini-Fracassini A. and Smith J. W.: *The structure and biochemistry of cartilage*, 168
Sevitt S.: *Reactions to injury and burns and their clinical importance*, 755
Shaftan G. W. and Gardner B.: *Quick reference to surgical emergencies* (ed.), 587
Shaw J.: *See* Bushe K. A. jt ed.
Shepherd J. A.: *A concise surgery of the acute abdomen*, 925
Sherlock S.: *See* Schaffner F. jt auth.
Shields T. W. and Ritts R. E.: *Bronchial carcinoma*, 588
Sillar W.: *A guide to disaster management based on proceedings of an inter-service conference held in the Walton Conference Centre, The Southern General Hospital, Glasgow, in September* 1973, *and a report on disaster response in America and Canada following the tornadoes of April* 1974 (ed.), 671
Silver H. K.: *See* Kempe H. jt auth.
Smillie I. S.: *Diseases of the knee joint*, 336
Smith J. W.: *See* Littler J. W. jt ed., Serafini-Fracassini A. jt auth.
Smith R.: *Surgical forum—the liver* (ed.), 754
Smith R. E. and Williams W. G.: *Surgery of the lung. The Coventry conference* (ed.), 252
Snell R. S.: *Clinical embryology for medical students*, 988
Solomon P. and Patch V. D.: *Handbook of psychiatry* (ed.), 418
Som A. L.: *Principles and practice of modern surgery*, 250
Spoerri O.: *See* Bushe K. A. jt ed.
Staehler W.: *See* Alken C. E. jt ed.
Stallworthy Sir John: *See* Howkings J. jt ed.
Stephenson H. E.: *Cardiac arrest and resuscitation*, 756
Stephenson K. L.: 1974 *Year book of plastic and reconstructive surgery* (ed.), 419
Stoll B. A.: *Mammary cancer and neuroendocrine therapy* (ed.), 250
Stuart A. E.: *See* Macpherson A. I. S. jt auth.
Sturdy D. E.: *Essentials of urology*, 335
Sumida S.: *Transfusion of blood preserved by freezing*, 415
Swanson A. B.: *Flexible implant resection arthroplasty in the hand and extremities*, 586
Thackray A. C. and Lucas R. B.: *Tumours of the major salivary glands (atlas of tumour pathology, second series)*, 671
Thornton H. L.: *Emergency anaesthesia* (ed.), 927
Todd M. E. and Wyburn G. M.: *Concise anatomy*, 927
Touloukian R. T. and Krizek T. J.: *Diagnosis and early management of trauma emergencies. A manual for the emergency service* (ed.), 416
Troelstra J. A.: *See* Jonxis J. H. P. jt ed.
Tubiana R.: *See* Hueston J. T. jt ed.
Umbach W. and Koepchen H. P.: *Central rhythmic and regulation: circulation, respiration, extrapyramidal motor system* (ed.), 167
Van Denmark P. J.: *See* Barnes I. J. jt auth.
Vander E.: *See* De Marneffe R. jt ed.
Vaughan D. and Asbury T.: *General opthalmology*, 502
Vischnevskiy A. A., Artobolevskiy I. I. and Bykhovskiy M. L.: *Machine diagnosis and information retrieval in medicine in the USSR* (ed.), 251

Reviews (Authors), *continued*
Visser H. K. A.: *See* Jonxis J. H. P. jt ed.
Vukovich V. C. and Grubb R. D.: *Care of the ostomy patient*, 83
Wakeley Sir Cecil, now revised by Bate J. G.: *The Faber medical dictionary* (ed.), 753
Waterhouse J. A. H.: *Cancer handbook of epidemiology and prognosis*, 168
Wells C., Kyle J. and Dunphy J. E.: *Scientific foundations of surgery* (ed.), 335
Williams W. G.: *See* Smith R. E. jt ed.
Wolcott M. W.: *Ferguson's surgery of the ambulatory patient* (ed.), 754
Wyburn G. M.: *See* Todd M. E. jt auth.
Wyke B.: *Ventilatory and phonatory control systems* (ed.), 755
Zenker R., Deucher F. and Schink W.: *Chirurgie der Gegenwart* (ed.), 83, 335, 416, 502
Zollinger R. M.: *See* Hardy J. D. jt ed.
Zuidema G. D.: *See* Ballinger W. F. jt ed.
Ribeiro C. D.: *See* Beard C. H. jt auth.
Rickford C. R. K. and Negus D.: The early detection of postoperative deep vein thrombosis: an assessment of Doppler ultrasound, physical examination and the temperature chart, 182
Ritchie J. K.: *See* Marks C. G. jt auth.
Rivlin S.: The surgical cure of primary varicose veins, 913
Robert Jones operation, modified, results of, for clawed hallux, 651
Roberts J. G., Keyser J. W. and Baum M.: Serum α-1-acid glycoprotein as an index of dissemination in breast cancer, 816
Roberts M. M. and Bathgate E. M.: The immune reaction to human breast cancer: a comparison of skin and leucocyte migration tests, 820
Roberts P. A.: *See* Browne C. H. jt auth.
Roberts V. C.: *See* Cotton L. T. jt auth.
Robertson J. C.: *See* Isherwood P. A. jt auth.
Robin P. E., Powell D. J., Waterhouse J. A. H. and Dalton G. A.: Trans-sphenoidal hypophysectomy in disseminated carcinoma of the breast, 85
Robinson K. P., Andrews B. G. and Vitali M.: Immediate operative fitting of upper limb prosthesis at the time of amputation, 634
Robinson V.: *See* Condon J. R. jt auth.
Rogers I. M.: *See* Reid D. R. K. jt auth.
Rokkanen P.: *See* Jäättelä A. jt auth.
Rosenberg I. L., Brennan T. G. and Giles G. R.: How tight should tension sutures be tied? A controlled clinical trial, 950
Rosenberg I. L.: *See also* Evans C. jt auth., Trindade L. M. jt auth.
Ross C. F. and Eley A.: Lymphosarcoma of the breast, 651
Rossi A.: *See* Isherwood P. A. jt auth.
Roux-en-Y anastomosis, antrectomy with, in treatment of peptic oesophagitis with stricture, 605
Royston C. M.: *See* George W. D. jt auth.
Royston C. M. S., Dowling B. L. and Spencer J.: Antrectomy with Roux-en-Y anastomosis in the treatment of peptic oesophagitis with stricture, 605
Rozycki Z. J.: *See* Trindade L. M. jt auth.
Rubber band, gangrene of tongue following self-application of, 956
  band ligation of haemorrhoids, long term review of results of, 144
  bullets, injuries caused by: report on 90 patients, 480
Rupture, bilateral simultaneous, of quadriceps tendons, 918
  caecal, due to colonic ileus, 383
  intrabiliary, of hydatid cyst of liver, 885
  of subcapsular haematoma of liver in case of eclampsia, 237
Rutherford W. H.: *See* Millar R. jt auth.

Sage R. H.: *See* Campbell D. J. jt auth.
Saharia P. C.: Carcinoma arising in thyroglossal duct remnant: case reports and review of the literature, 689
Sames P.: The use of the vas deferens in inguinal herniorrhaphy, 495
Sanderson P. J.: *See* Gilmore O. J. A. jt auth.
Sankaran S. and Walt A. J.: The natural and unnatural history of pancreatic pseudocysts, 37
Saphenofemoral junction, technique for re-exploration of, for recurrent varicose veins, 745
Satake K., Sowa M., Kamashita K., Kamino K., Kinoshita J., Kato M. and Umeyama K.: Carcinoma of the duodenum: its preoperative diagnosis, 973
Saphenous vein bypass grafts for obstruction of superficial femoral artery, reason for early failure of: undetected aorto-iliac insufficiency, 567
Scanning, computer-assisted parathyroid, localization of parathyroid adenomas by, 553
Scars, normal and hypertrophic, and keloid, collagen biosynthesis in, as function of duration of scar, 741
Schalm S. W., Popescu D. T., van der Waay D., Krom R. A. F., Hendriks W. D. H., Terpstra J. L. and Jerusalem C.: Orthotopic liver transplantation: an experimental study on the prevention of infections with Gram-negative organisms, 513
Schofield J. D.: *See* Craig R. D. P. jt auth.
Schraibman I. G., Mott D., Naylor G. P. and Charlesworth D.: Comparison of impedance and strain gauge plethysmography in the measurement of blood flow in the lower limb, 909
Scintigraphy, skeletal, significance of occult skeletal metastases, detected by, in patients with otherwise apparently 'early' mammary carcinoma, 694
Scott C. C. (the late) and Guthrie T. D.: Environmental tests of linear flow ventilation for an operating theatre, 462
Screen filtration pressure of blood in experimental hypotension, effect of heparin and of acid-citrate-dextrose solution on, 713
Screening for breast cancer, feasibility of, 804
'Second look operation', is [it] justified in suspected recurrences after abdominal cancer surgery? 830
'Second look surgery', is [it] justified in suspected recurrences of cancer of stomach? 226
Secretion, gastric acid, following renal transplantation, 737
  gastric, relationship of anaemia to, more than 15 years after vagotomy and gastro-enterostomy, 356
Seidman L. H.: *See* Gordon D. L. jt auth.
Selective vagotomy and pyloroplasty, recurrence of gastric ulcer after, for chronic uncomplicated gastric ulcer: 5–10 year follow-up, 875
Sells R. A.: *See* McArthur P. jt auth.
Sellwood R. A.: *See* England P. C. jt auth.
Sengupta R. P., So S. C. and Perry R. H.: Nodular fasciitis: an unusual cause of extradural spinal cord compression, 573
Sengupta R. P.: *See also* Ramani P. S. jt auth.
Septic shock, 777
Septicaemia, fatal *Clostridium welchii*, following acute cholecystitis, 518
  Gram-negative, in surgical practice, 773
Sex hormones in breast disease, 806
Sharma L. K.: *See* Prakash A. T. M. jt auth.
Sharma M. M.: *See* Pendse A. K. jt auth.
Sharp C. A.: *See* Bartzokas C. A. jt auth.
Shaw R. E.: *See* Parker R. W. jt auth.
Shaw W.: *See* Gierson E. D. jt auth.
Shields R.: *See* Smith A. H. jt auth., McArthur P. jt auth.
Shock, septic, 777
Shorey B. A.: Pilonidal sinus treated by phenol injection, 407
Shukla H. S.: *See* Das P. jt auth.
Siddons H. and Nowak K.: Surgical complications of implanting pacemakers, 929
Sigmoid diverticulitis, ureteric obstruction due to, 247
Simpson A. and Srivastava V. K.: Temporary transcaecal ileal diversion in prevention of anastomotic leak in planned colonic surgery (an alternative to proximal colostomy), 243
Singer A. M.: *See* Blamey R. W. jt auth.

Sinus, pilonidal, treated by phenol injection, 407
Skeletal metastases, occult, significance of, detected by skeletal scintigraphy, in patients with otherwise apparently 'early' mammary carcinoma, 694
Skin and leucocyte migration tests, comparison of: immune reaction to human breast cancer, 820
  wounds, healing, effect of metal clips on tensile properties of, 945
Skin-lined hemithorax, construction of, in pigs, 351
Skinner D. B.: *See* Moossa A. R. jt auth.
Skinner J. M., Heenan P. J. and Whitehead R.: Atrophic gastritis in gastrectomy specimens, 23
Skinner J. M.: *See also* Brock, Lord jt auth.
Skinner L. G.: *See* England P. C. jt auth.
Slack R. W. T.: The survival rate of men with carcinoma of the breast: a long term follow-up study, 963
Smith A. H. and Shields R.: The effect of raising the concentration of potassium in the blood or intestinal lumen on the transport of potassium in the dog intestine, 455
Smith A. H.: *See also* Hill G. L. jt auth.
Smith I. S.: *See* Young S. jt auth.
Smith K.: *See* Hancock B. D. jt auth.
Smith P. G.: *See* Chan P. S. F. jt auth.
So S. C.: *See* Sengupta R. P. jt auth.
Sodium cholate infusion and Burhenne catheter, experience with: removal of retained gallstones from common bile duct, 520
  total exchangeable, total body water, and total body potassium, long term changes in, before and after ileostomy, 524
Sokhi G. S., Morrice J. J., McGee J. O'D. and Blumgart L. H.: Congenital hepatic fibrosis: aspects of diagnosis and surgical management, 621
Solcoseryl, intra-arterial infusion of: clinical trial of method of treatment for pre-gangrene of lower limb, 337
Sowa M.: *See* Satake K. jt auth.
Spencer J.: *See* George W. D. jt auth., Royston C. M. S. jt auth.
Spencer J. D.: Postvagotomy dysphagia, 354
Spermatogenesis, normal, triorchidism with: unusual cause for failure of vasectomy, 633
Sphincter, internal, and Lord's procedure for haemorrhoids, 833
  lower oesophageal, response of, to maximal doses of pentagastrin, 11
  pressure, lower oesophageal, after meals, relationship between changes in plasma gastrin and, 15
Spinal cord compression, extradural, unusual cause of: nodular fasciitis, 573
  interbody fusion, cervical, with Kiel bone, 147
  osteophytes, intra-abdominal symptoms arising from, 320
  tumours, raised intracranial pressure due to: 3 rare cases with probable common mechanism, 92
Spine, ossification in extradural fat in Paget's disease of, 571
Splenic-gonadal fusion, 624
Srivastava V. K.: *See* Simpson A. jt auth.
Stab wounds, abdominal, selective surgery for, 750
Starch granulomas, identification of talc on surgeons' gloves and in tissue from, 941
Steinberg D. M., Liegois H. and Alexander-Williams J.: Long term review of the results of rubber band ligation of haemorrhoids, 144
Sterilization, surgical, by vasectomy and its effect on structure and function of testis in man, 59
Stomach, cancer of, is 'second look surgery' justified in suspected recurrence of? 226
Stone, hanging bladder, formed around Mersilene mesh, 413
Storm F. K.: *See* Gierson E. D. jt auth.
Strain gauge plethysmography, impedance and, comparison of, in measurement of blood flow in lower limb, 909
Stricture, antrectomy with Roux-en-Y anastomosis in treatment of peptic oesophagitis with, 605
Stricture(s), bilateral idiopathic parotid duct, 468
  peptic oesophageal, management of, 448
Strunin J. M.: *See* Strunin L. jt auth.
Strunin L., Knights K., Strunin J. M. and Ward M. E.: General anaesthesia during early pregnancy, 471
Subphrenic abscess in children, 305
Subrahmanian M. V., Rajendraprasad G. B. and Rao B. D.: Bilateral extradural haematomas, 397
Suleman M. I.: *See* Condon J. R. jt auth.
Sumitswan S.: *See* Welch T. P. jt auth.
Superficial femoral artery, reason for early failure of saphenous vein bypass grafts for obstruction of: undetected aorto-iliac insufficiency, 567
Surgical masks, of varying design and composition, efficiency of, 936
Surgical Research Society, 151, 653
Sussman M.: *See* Vajrabukka T. jt auth.
Suture(s) material, does choice of, affect incidence of wound infection? 952
  tension, how tight should [they] be tied? A controlled clinical trial, 950
Sweeney M.: *See* Norton L. W. jt auth.
Sympathectomy, phenol, in treatment of intermittent claudication: controlled clinical trial, 68
Synchronous combined excision, complications of, for adenocarcinoma of rectum at St Mark's Hospital, 901
Syndrome, Gardner's, epidermoid cysts, polyposis coli and, 387

Talc, identification of, on surgeons' gloves and in tissue from starch granulomas, 941
Tamponade, fatal cardiac, and other mechanical complications of central venous catheters, 6
Taylor L.: *See* Charlesworth D. jt auth.
Taylor R. M. R.: *See* Britton D. C. jt auth.
Taylor T. V., Pullan B. R., Elder J. B. and Torrance B.: Observations of gastric mucosal blood flow using ^{99}Tc^{m} in rat and man, 788
^{99}Tc^{m}, observations of gastric mucosal blood flow using, in rat and man, 788
  phosphate bone scan, application of, to study of breast cancer, 201
Techniques, comparison of one layer and two layer, for colorectal anastomosis, 135
Tehrani M. A.: *See* Ledingham I. McA. jt auth.
Temperature(s), importance of environmental conditions, especially, in operating room and intensive care ward, 252
  peripheral and central, observations on, with particular reference to occurrence of vasoconstriction, 589
Tendons, quadriceps, bilateral simultaneous rupture of, 918
Tension sutures, how tight should [they] be tied? A controlled clinical trial, 950
Terblanche J., Hickman R. and Uys C. J.: Renal transplantation in the unimmunosuppressed pig: an abnormal response, 474
Terblanche J.: *See also* Wheatley I. C. jt auth.
Terpstra J. L.: *See* Schalm S. W. jt auth.
Tervo T.: *See* Jäättelä A. jt auth.
Testa H. J.: *See* Watson A. jt auth.
Testis, surgical sterilization by vasectomy and its effect on structure and function of, in man, 59
  torsion of: review of 22 cases, 57
Thavendran A., Vijayaragavan A. and Rasaretnam R.: Selective surgery for abdominal stab wounds, 750
Thomas W.: *See* Gordon D. L. jt auth.
Thomson J. A., Kennedy J. S., Browne M. K. and Hutchison J.: Secondary carcinoma of the thyroid gland, 692
Thomson J. P. S.: *See* Faris I. jt auth.
Thomson W. H. F.: The nature of haemorrhoids, 542
Thrombosis, deep vein, small doses of subcutaneous sodium heparin in prevention of, after elective hip operations, 348

Thrombosis(es), popliteal arterial, complete disappearance of, in 2 patients, 141
postoperative deep vein, early detection of: assessment of Doppler ultrasound, physical examination and temperature chart, 182
Thynne G. S. J.: *See* Millis R. R. jt auth.
Thyroglossal duct remnant, carcinoma arising in: case reports and review of literature, 689
Thyroid cancer, non-surgical treatment of, 769
cancer, surgery of, 765
cancer: twenty years' experience in general hospital, 207
gland, aetiology and diagnosis of malignant tumours of, 760
gland, secondary carcinoma of, 692
malignancy, pathology of, 757
nodules, cystic, 205
report of family with inherited medullary carcinoma of, and phaeochromocytoma, 264
Thyrotoxicosis, surgical treatment of: results of 272 operations with special reference to preoperative treatment with anti-thyroid drugs and L-thyroxine, 683
whither? 673
L-Thyroxine, results of 272 operations with special reference to preoperative treatment with anti-thyroid drugs and: surgical treatment of thyrotoxicosis, 683
Tinckler L.: A colostomy/ileostomy construction clamp, 246
Tiwari I. N.: *See* Gupta S. D. jt auth.
Todd-Pokropek A.: *See* Ell P. J. jt auth.
Toenail, ingrowing, surgical management of, 407
Tongue, gangrene of, following self-application of rubber band, 956
Topical cephaloridine, controlled clinical trial against: povidone-iodine for control of surgical wound infection, 292
Torrance B.: *See* Taylor T. V. jt auth., Watson A. jt auth.
Torsion of testis: review of 22 cases, 57
Transcaecal ileal diversion, termporary, in prevention of anastomotic leak in planned colonic surgery (alternative to proximal colostomy), 243
Transdiaphragmatic approach to heart, 731
Transplantation, orthotopic liver: experimental study on prevention of infections with Gram-negative organisms, 513
orthotopic liver, utilizing vascular stapling instrument, 438
prediction of kidney viability before, 810
renal, gastric acid secretion following, 737
renal, in unimmunosuppressed pig: abnormal response, 474
Trans-sphenoidal hypophysectomy in disseminated carcinoma of breast, 85
Trauma, blunt, abdominal lavage in, 121
surgical, effect of, on plasma concentrations of cyclic AMP and cortisol, 441
Traumatic haemobilia, 234
Trindade L. M., Rosenberg I. L., Rozycki Z. J. and Giles G. R.: The response of the lower oesophageal sphincter to maximal doses of pentagastrin, 11
Triorchidism with normal spermatogenesis: unusual cause for failure of vasectomy, 633
Tryfronas G. and Young D. G.: Extrinsic duodenal obstruction in infants and children, 125
Tsega E.: Pneumatosis cystoides intestinalis with unexplained ascites in Ethiopian patients, 379
Tubercle bacilli, demonstration of, in tissues and experimental production of hyperplastic enteric lesions: abdominal tuberculosis, 610
Tuberculosis, abdominal: demonstration of tubercle bacilli in tissues and experimental production of hyperplastic enteric lesions, 610
primary gastric: case report, 618
Tuberculous peripheral lymphadenitis in Igbos of Nigeria, 323
Tumours, malignant, of thyroid gland, aetiology and diagnosis of, 760
Tumours, spinal, raised intracranial pressure due to: 3 rare cases with probable common mechanism, 92

Ulcer, duodenal, effect of size of gastric outlet on gastric emptying after vagotomy for, 879
gastric, recurrence of, after selective vagotomy and pyloroplasty for chronic uncomplicated gastric ulcer: a 5–10 year follow-up, 875
peptic, gastric mucosal resection in treatment of: 1–10 year clinical follow-up, 608
Ulceration, indomethacin-induced gastric, decreased incidence of, in rats by bile duct diversion, 113
Ultrasound assessment and angiography, relationship between, in occlusive arterial disease of lower limb, 64
Doppler, physical examination and temperature chart, assessment of: early detection of postoperative deep vein thrombosis, 182
Umeyama K.: *See* Satake K. jt auth.
Ureteric obstruction due to sigmoid diverticulitis, 247
Urological practice, analgesic abuse in, 298
Utsunomiya J. and Nakamura T.: The occult osteomatous changes in the mandible in patients with familial polyposis coli, 45
Uys C. J.: *See* Terblanche J. jt auth.

Vagotomy, effect of size of gastric outlet on gastric emptying after, for duodenal ulcer, 879
and gastro-enterostomy, relationship of anaemia to gastric secretion more than 15 years after, 356
proximal gastric, motility changes in antrum after, 215
selective, and pyloroplasty, recurrence of gastric ulcer after, for chronic uncomplicated gastric ulcer: 5–10 year follow-up, 875
Vajrabukka T., Bloom A. L., Sussman M., Wood C. B. and Blumgart L. H.: Postoperative problems and management after hepatic resection for blunt injury to the liver, 189
Vallidis E. and Papalexandris N.: Traumatic haemobilia, 234
van der Waay D.: *See* Schalm S. W. jt auth.
Varices, bleeding oesophageal, abdominal approach for ligation of, 108
Varicose veins, clinical trial designed to discover if primary treatment of, should be by Fegan's method or by operation, 72
veins, primary, surgical cure of, 913
veins, recurrent, technique for re-exploration of saphenofemoral junction for, 745
Vas deferens, use of, in inguinal herniorrhaphy, 495
Vascular stapling instrument, orthotopic liver transplantation utilizing, 438
Vasectomy, surgical sterilization by, and its effect on structure and function of testis in man, 59
unusual cause for failure of: triorchidism with normal spermatogenesis, 633
Vasoconstriction, observations on peripheral and central temperatures with particular reference to occurrence of, 589
Vasudevan K.: *See* Dutta T. jt auth.
Veins, primary varicose, surgical cure of, 913
recurrent varicose, technique for re-exploration of saphenofemoral junction for, 745
Venables C. W.: *See* Wheldon E. J. jt auth.
Venous pressure, peripheral, some observations on, using non-invasive technique: preliminary report, 259
Venous Thrombosis Clinical Study Group: Small doses of subcutaneous sodium heparin in the prevention of deep vein thrombosis after elective hip operations, 348
Ventilation, linear flow, environmental tests of, for operating theatre, 462
Vijayaragavan A.: *See* Thavendran A. jt auth.
Vitali M.: *See* Robinson K. P. jt auth.
Vogelfanger I. J.: *See* Barron P. T. jt auth.
Volvulus of gastric fundus, case of haemorrhage from, 224

Waddell W. G.: *See* Barron P. T. jt auth.
Wade J. S. H.: The aetiology and diagnosis of malignant tumours of the thyroid gland, 760
Walt A. J.: *See* Sankaran S. jt auth.
Ward C. M.: Injury of the facial nerve during surgery of the parotid gland, 401
Ward M. E.: *See* Strunin L. jt auth.
Water, total body, total exchangeable sodium and total body potassium, long term changes in, before and after ileostomy, 524
Waterhouse J. A. H.: *See* Robin P. E. jt auth.
Watson A., Bone D. E., Testa H. J. and Torrance B.: The value of the radio-isotope hepatogram in the jaundiced patient, 781
Watson W. W.: *See* Himal H. S. jt auth.
Watts G. T.: *See* Keighley M. R B. jt auth.
Webster D. J. T.: Carcinoma of the pancreas and periampullary region: a clinical study in a district general hospital, 130
Welch T. P. and Sumitswan S.: Acute segmental ischaemic enteritis in Thailand, 716
Wheatley I. C., Barbezat G. O., Hickman R. and Terblanche J.: The effect of acute ethanol administration on the exocrine pancreatic secretion of the pig, 707
Wheldon E. J., Venables C. W. and Johnston I. D. A.: The relationship of anaemia to gastric secretion more than 15 years after vagotomy and gastroenterostomy, 356
White blood cells, peripheral, amino acid incorporation by, in man: measurement of immune response to allograft, 863
  cell count, assessment of value of, in management of suspected acute appendicitis, 906
White M.: *See* Doran F. S. A. jt auth.
Whitehead R.: *See* Skinner J. M. jt auth.
Whyte A. S.: *See* Imrie C. W. jt auth.
Williams D. F.: *See* Harrison I. D. jt auth.
Williams E. D.: The pathology of thyroid malignancy, 757
Williams H. I.: *See* Clarke P. R. R. jt auth.
Williams J. S.: *See* Hines J. R. jt auth.
Williams R. E.: *See* Page R. E. jt auth.
Williamson R. C. N.: The management of peptic oesophageal stricture, 448
Windle R. and Peacock J. H.: Prognosis after portocaval anastomosis: a 15-year follow-up, 701
Windsor C. W. O.: *See* Kingston R. D. jt auth.
Wood C. B.: *See* Vajrabukka T. jt auth.
Wosornu L.: The construction of a skin-lined hemithorax in pigs, 351
Wound(s), abdominal stab, selective surgery for, 750
  healing skin, effect of metal clips on tensile properties of, 945
  infection, does choice of suture material affect incidence of? 952
  infection, surgical, povidone-iodine for control of: controlled clinical trial against topical cephaloridine, 292
  infections due to *Bacteroides fragilis* following intestinal surgery, 375
  laparotomy, controlled clinical trial of three methods of closure of, 823
  management, perineal, controlled trial of three different methods of, following excision of rectum, 287
Wright N. A.: *See* Britton D. C. jt auth.
Wyatt A. P.: Prolonged symptomatic and radiological remission of colonic gas cysts after oxygen therapy, 837

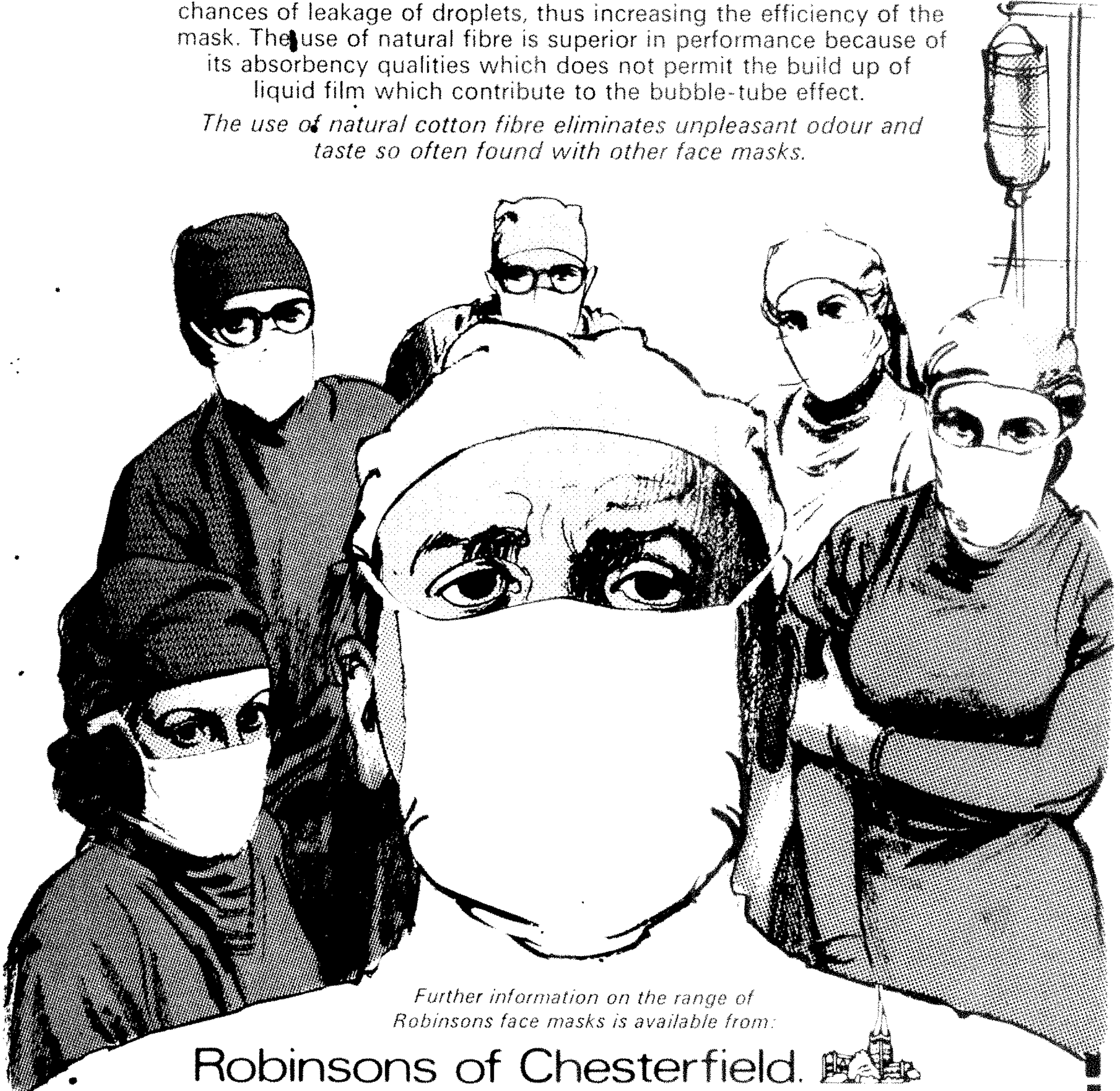
Xanthogranulomatous pyelonephritis: report of 2 cases, 563

Yamashita K.: *See* Satake K. jt auth.
Yeadon A.: *See* Mouzas G. L. jt auth.
Young D. G.: *See* MacKenzie M. jt auth., Tryfonas G. jt auth.
Young S., Smith I. S., O'Connor J., Bell J. R. and Gillespie G.: Results of surgery for Crohn's disease in the Glasgow region, 1961–70, 528

The facts behind the mask

The Cestra mask has high absorbency qualities and high filtration efficiency. Made from cotton fibre, it is soft and extends well back over the cheeks and under the chin, covering a larger area than many other masks. The extensive facial coverage decreases the chances of leakage of droplets, thus increasing the efficiency of the mask. The use of natural fibre is superior in performance because of its absorbency qualities which does not permit the build up of liquid film which contribute to the bubble-tube effect.

The use of natural cotton fibre eliminates unpleasant odour and taste so often found with other face masks.



Further information on the range of Robinsons face masks is available from:

Robinsons of Chesterfield.

Robinson & Sons Limited, Wheat Bridge, Chesterfield S40 2AD.

NAME

POSITION

ADDRESS

SIEMENS

DIATHERMY EQUIPMENT
for modern
ELECTRO-SURGICAL
TECHNIQUES

Available in various designs such as

TROLLEY MOUNTED,
CEILING SUSPENSION
or installation in the
OPERATING THEATRE WALL

Full details available on request
SIEMENS

Siemens Limited Medical, Electro-Medical Division
Heron House, 109 Wembley Hill Road,
Wembley HA9 8BZ. Telephone 01 903 0418

Branches in Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester, Newcastle and Reading. Agents in Belfast.

CHARLES C THOMAS • PUBLISHER

CURRENT MANAGEMENT OF TRAUMA IN SURGERY AND GENERAL PRACTICE *edited by* **Teruo Matsumoto**, *The Hahnemann Medical College and Hospital of Philadelphia, Philadelphia, Pennsylvania. (29 Contributors)* The purpose of this text is to provide comprehensive understanding of the minimum but essential didactic and practical methods of trauma management. It is designed to survey current concepts in the management of various aspects of trauma as well as complications and shock related to these conditions. Particular emphasis is placed on the practical aspects of pathophysiology, new diagnostic techniques and the best approach for the practicing surgeon. *'75, 400 pp. (5 3/8 x 8 1/2), 89 il. $23.50*

CLINICAL APPLICATIONS OF ZINC METABOLISM *edited by* **Walter J. Pories**, *Case Western Reserve Univ., Cleveland, Ohio;* **William H. Strain**, *Cleveland Metropolitan General Hospital, Cleveland, Ohio;* **Jeng M. Hsu**, *Johns Hopkins Univ., Baltimore, Maryland; and* **Raymond L. Woosley**, *Meyer Laboratories, Fort Lauderdale, Florida. Foreword by* **Bert L. Vallee.** *(45 Contributors)* Many clinical applications of zinc therapy are detailed in this volume including the critical importance of zinc therapy in the two basic metabolic processes of growth and repair. The nutritional effects of zinc in man and biochemical and metabolic effects of zinc deficiency are discussed. Other topics include the role of zinc in protein synthesis, zinc therapy in surgical patients and in the management of severely burned patients. *'75, 320 pp. (6 3/4 x 9 3/4), 79 il., 80 tables, $28.50*

PROBLEMS OF RECURRENT HERNIA *by* **Robert C. Kimberly**, *Johns Hopkins Medical School, Baltimore, Maryland.* With emphasis on treatment of the patient as well as of the hernia, this book will aid surgeons in managing the problem of recurrent hernia. The causes of the recurrence of a hernia are discussed with stress upon the role of infection and pulmonary complications. Preoperative preparation is among the general principles in the management of recurrent hernia that are considered. Recurrent inguinal, femoral, ventral, diaphragmatic and muscle hernias are discussed separately. The use of prosthetic materials in recurrent hernia is also covered. This volume will help to make difficult operations easy. *'75, 76 pp. (5 3/8 x 8 1/2), 21 il., $6.50, paper*

PATHOLOGY AND SURGERY OF THE SALIVARY GLANDS *by* **Jose Yoel**, *Rawson Hospital, Municipal Post Graduate School of Medicine, Buenos Aires, Argentina. Forewords by* **Pierre Cernea, John Conley, Hector Marino** *and* **S. L. Perzik.** Anatomy, physiology, pathology and semiology, instrumental and radiological exploration, and medical and surgical treatment of salivary gland diseases have been extensively covered in this book. Clear anatomophysiologic sketches and magnificent illustrations of the operative stages clearly depict what the surgeon actually sees in the operative field. Fundamental concepts of embryology, histology, physiology, endocrinology, and general pathology of the salivary glands and their diagnostic methods are reviewed. *'75, 1446 pp. (7 x 10), 2074 il. (7 in full color), 6 tables, $132.50*

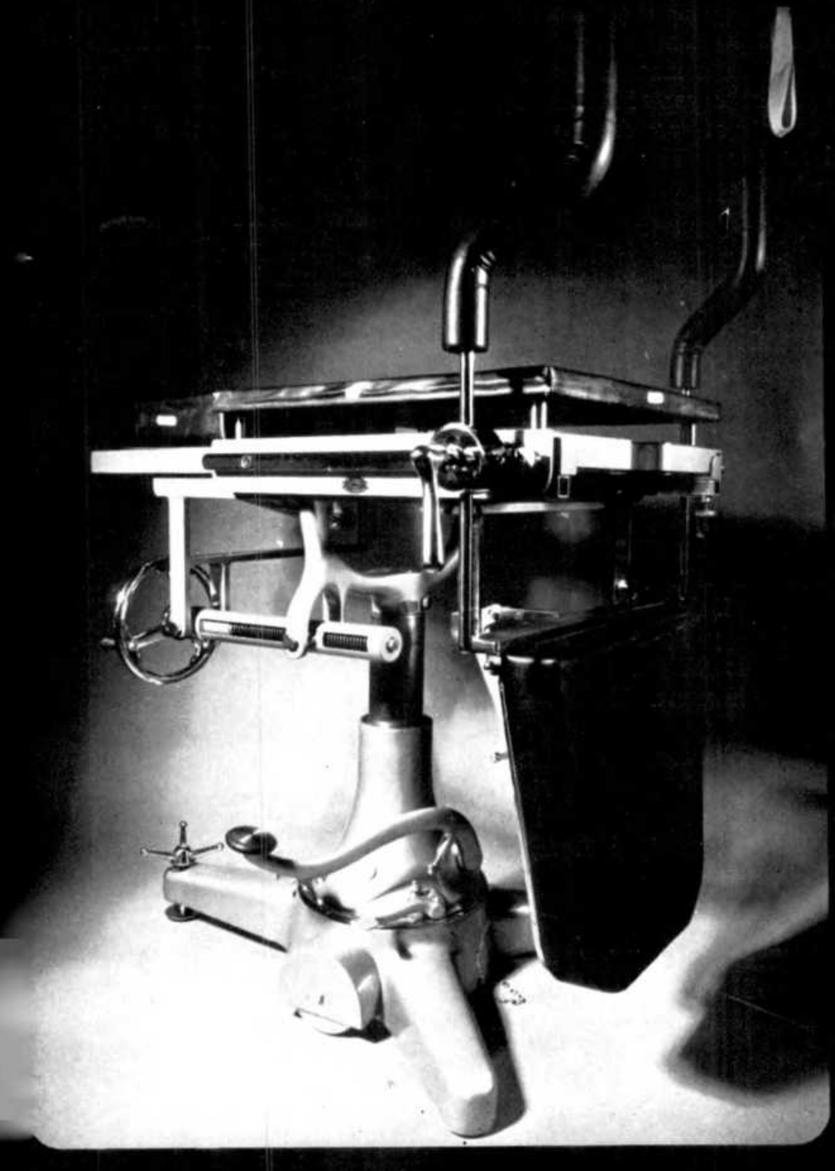
NORMAL AND ABNORMAL GROWTH OF THE PROSTATE *edited by* **Martin Goland**, *Southwest Foundation for Research and Education, San Antonio, Texas. (90 Contributors)* This text summarizes current knowledge concerning the prostate gland. It is divided into sections covering such areas as embryology, development and pathology of the prostate gland, metabolism of steroids in prostatic tissue, regulation of prostatic metabolism, ligandmacromolecular binding and transport mechanisms, and experimental and clinical approaches to the prostatic cavity. Some of the chapter topics included in these sections are the fetal and neonatal prostate, androgen dynamics *in vitro* in the human prostate gland, hormonal regulation of RNA synthesis, prolactin and the prostate, and endocrine profiles in carcinoma of the prostate. *'75, 964 pp., 451 il., 123 tables, $48.75*

ANKLE FRACTURES: Treatment Without Casts *by* **Leo K. Cooper**, *Gary, Indiana.* The cases and treatments cited stem from a practice of this treatment with the scope being limited to fractures involving the ankle joint. Various types of fractures which occur in the ankle joint and at times are associated with severe injuries of the foot are represented along with treatment, physiology, complications and case studies. The author wishes to stress the importance of early, rapid, accurate fixation of fractures of the ankle and rapid restoration of the physiology of the extremity. This is characterized by early motion of the muscles and joints which in turn improve the circulation and promote rapid healing. *'74, 124 pp. (8 1/2 x 11), 172 il., $18.50*

Orders with remittance sent by air, postpaid

301-327 East Lawrence Avenue • Springfield • Illinois • 62717 • USA

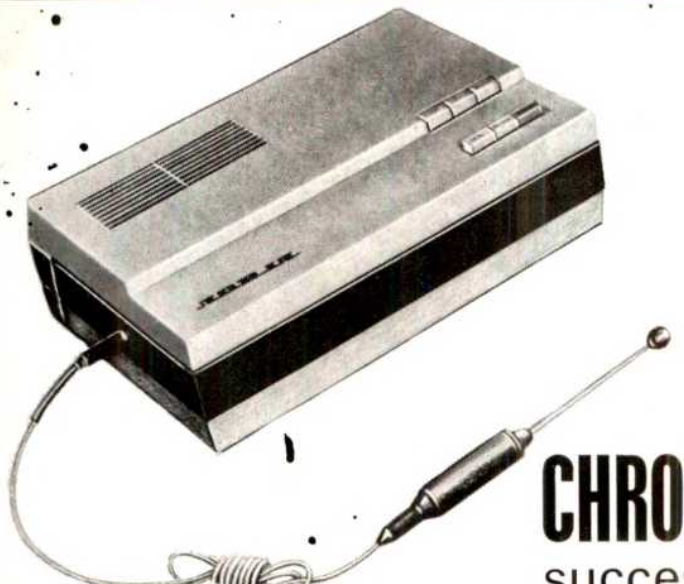
THACKRAY



Belfast table

A table for perineal and general surgery which is designed to allow the patient to be placed in lithotomy position without being lifted or pulled down the table.

ackray Limited, Head Office: P.O. Box 171 Park Street, Leeds LS1 1RQ



The LOR-1A
APPARATUS

CHRONIC TONSILLITIS
successfully treated by
ultrasonic therapy

The LOR-1A apparatus produces mechanical vibrations of ultrasonic frequency which have a therapeutic effect on infected tonsils. Clinical tests have shown 75% success in patients treated. Advantages of the LOR-1A are its small dimensions and low weight (less than 5 kg) and its proven safety, reliability and ease of operation. Small ultrasonic generator of low operating voltage permits direct treatment to tonsils.

Detailed information available from

V/O MEDEXPORT

31 Kakhovka, Moscow 113461, USSR. Telex 7247
Tel: 121-01-54

BURNS including Thermal Injury

The Journal of the International Society for Burn Injuries

Editor, J. E. LAING, FRCS

To counter the high mortality and morbidity caused by burn injuries needs the teamwork of a wide range of specialists: treatment of the patient can involve plastic, paediatric and orthopaedic surgeons, biologists, immunologists and bacteriologists, while the rehabilitation of the patient can need the efforts of occupational therapists, physiotherapists, psychiatrists and social workers. This new journal is published to foster the exchange of information amongst all those engaged in preventing and minimizing the effects of burn injuries. BURNS is sponsored by the International Society for Burn Injuries, whose aims are to transcend national boundaries in improving the prevention and care of burns by education, research, practical advice and assistance, and the encouragement of cooperation between all countries and all specialists.

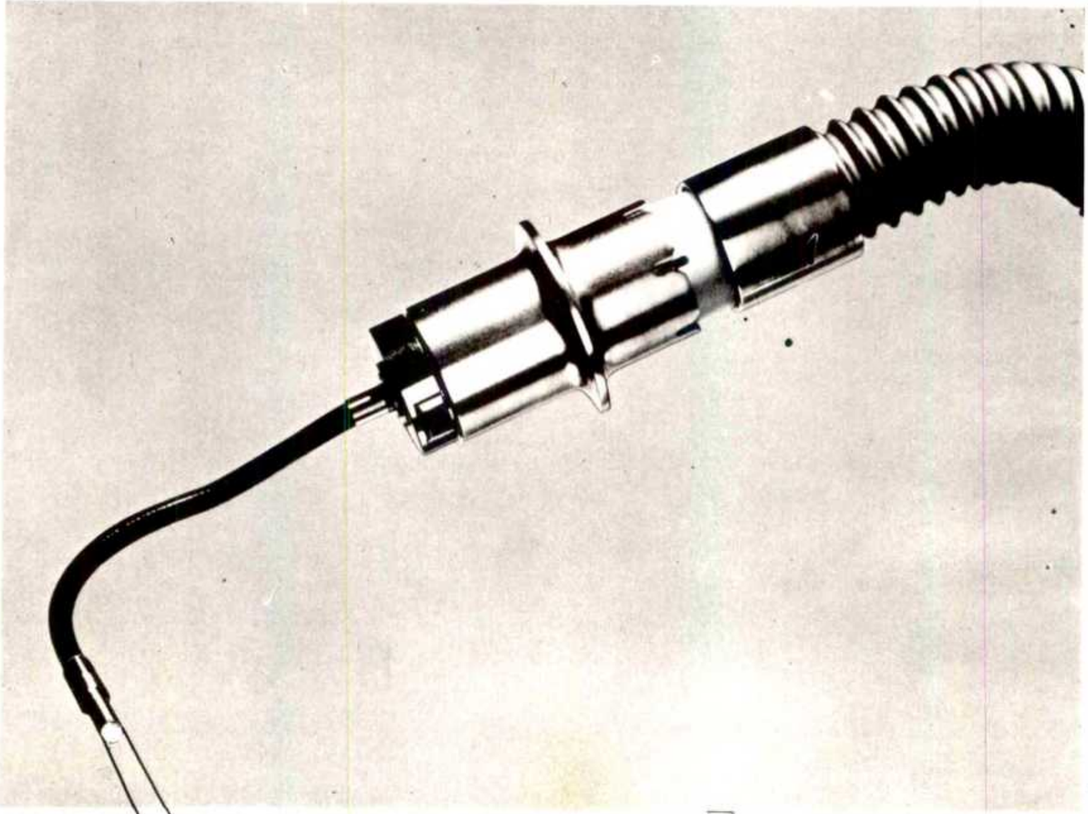
Published Quarterly

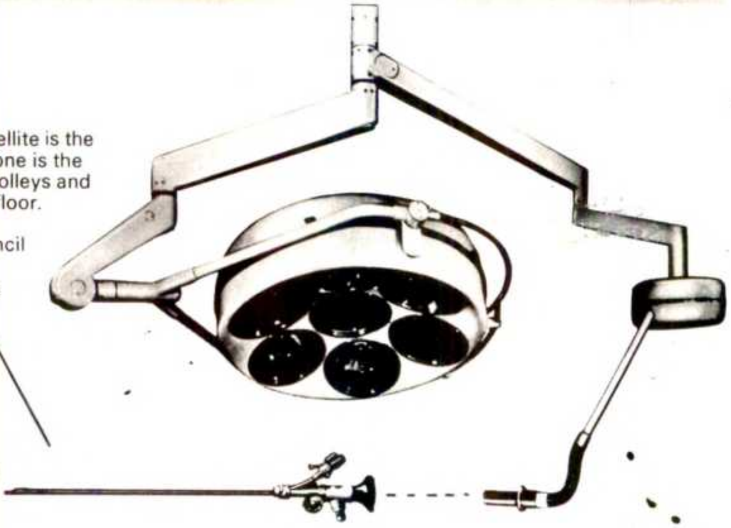
Annual subscription: £10·00 (post free)
Single Numbers: £3·00 (post free)

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

new

FLEXIBLE PENCIL LIGHT





The Boston lamp with its GFO Satellite is the ideal endoscopic light source. Gone is the need for a separate source, for trolleys and mains cables trailing across the floor.

Illustrated above is a flexible pencil light, ideal for Neuro and ENT surgery, shown connected to the GFO Satellite.

Most glass-fibre endoscopic instruments can be connected in this way.

SIEMENS

Siemens Limited Medical, Surgical Division

15/18 Clipstone Street, London, W1P 8AE, 01-580 2464
Branches in *Aberdeen, Birmingham, Bristol, Bury St. Edmunds, Dublin, Edinburgh, Glasgow, Leeds, Liverpool, Manchester and Reading.*
Agents in *Belfast, Newcastle and Newport.*

Operational Flexibility

The dual channel ACM F9A and F9R are the world's most advanced operating coloscopes. With either, a surgeon has at his fingertips a range of capabilities and techniques.

The F9A has a useful length of 165 cm., sufficient for a variety of therapeutic procedures up to the caecum, while the shorter (105 cm.) F9R, with a softer shaft, can cover most of the known pathology of the colon.

Even the most delicate and precise procedures become routine with the F9A and F9R. Both models feature ACM's unique twin channel design (7 Fr. and 12 Fr.), each with independent suction, which permits the surgeon to select any combination of snares, forceps, electrodes, retrievers, cytology brushes etc., that he needs.

And of course, both incorporate all the advanced features of other ACM endoscopes, including :–

- *Polydirectional distal tip with 320° deflection and single-lever control
- *Separate channel for air, CO_2 or water
- *Wide angle, fixed focus optics
- *Clear, bright circular image with 12X magnification

The F9A and F9R are supported by a full range of accessories and will accept the unique ACM teaching attachment. There are single channel models too, the ACM F9S and F9L, for diagnosis and less demanding surgica procedures.

For further details of the ACM F9 range, the world's most versatile coloscopes, please telephone or write to us.

Please tell me more about ACM endoscopes
I would like literature only ☐
Please arrange a visit by a technical representative
My telephone number is ☐
Name
Address

B.J.S. 12-75

ACM

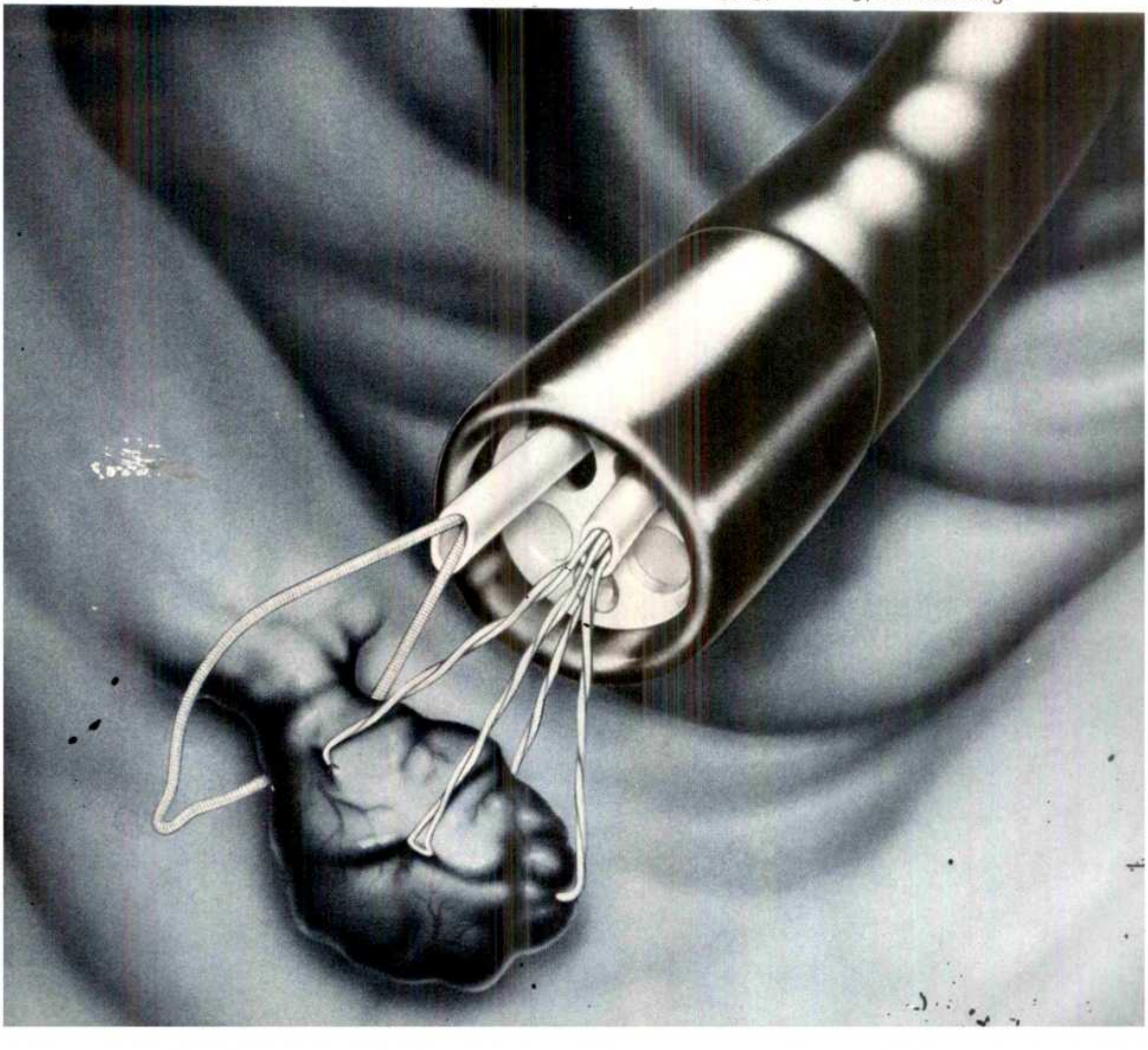
WAPPLER ENDOSCOPY LIMITED

Park House, 22 Park Street, Croydon, Surrey, CRO OYH
Telephone : 01-686 4241

WAPPLER Endoscopy Limited

ACM Endoscopes – clearly the best

ACM endoscopes for gastro-enterology, bronchoscopy, urology, gynaecology and teaching.



CHEST INJURIES

A Guide for the Accident Department

G. KEEN, MS, FRCS
Thoracic and Cardiac Surgeon, United Bristol Hospitals and Frenchay Hospital; Clinical Lecturer in Thoracic Surgery, University of Bristol

With a Foreword by
RONALD BELSEY, MS, FRCS

Contents:
Introduction; Assessment of patients with chest injuries; Management of pain; Management of the airway and of ventilation; Radiological features of chest injuries; Traumatic emphysema; Traumatic pneumothorax and haemothorax; Skeletal injuries and flail chest; Fractured ribs and sternum; Lung injuries; Tracheobronchial injuries; Traumatic rupture of the diaphragm; Traumatic chylothorax; Oesophageal injuries; Closed injuries of the heart and pericardium; Penetrating wounds of the heart and great vessels; Penetrating wounds of the chest; Closed injuries of the thoracic aorta; Indications for thoracotomy following chest injuries; Bibliography; Index.

186 pages 78 illustrations £7·00 net
ISBN 0 7236 0413 4

JOHN WRIGHT
42–44 Triangle West, Bristol BS8 1EX

Our experience is something you can rely on

Remploy's contribution to Orthotics goes far beyond providing a comprehensive range of orthopaedic equipment.

Remploy are able to offer a unique measuring and fitting service for all their appliances and footwear, and have produced two orthopaedic brochures which are an invaluable aid to work in this field. Rely on this experience and send for literature, now.

Remploy

An exceptional name in Orthotics

A.H. Knight Remploy Limited (Orthopaedic Division),
Remploy House, 415 Edgware Road, Cricklewood,
London NW2 6LR. Telephone: 01-452 8020.

FIGHT BACK AGAINST CANCER

It is good to remember that most people live their lives untouched by any form of cancer.

But as all too many are aware, cancer is something that casts its shadow far beyond those it directly affects. That is why so many people think it right to help the urgent work of the Imperial Cancer Research Fund.

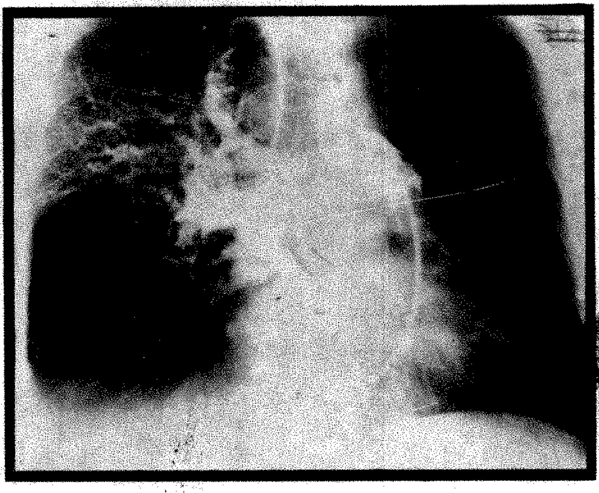
From our discoveries in the past has come much of today's hope for sufferers. To go forward with our research for future alleviation, we ask *your* help in the present.

The main laboratories at Lincoln's Inn Fields

IMPERIAL CANCER RESEARCH FUND

Donations will be most gratefully received by the Appeals Secretary,
Room 164/4, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX

RED ALERT!



When acute massive pulmonary embolism occurs put them on Kabikinase to dissolve the embolus and the still threatening deep vein thrombus and restore the flow. (Lysis achieved, anticoagulate with heparin to prevent rethrombosis.)

"We believe that the current treatment of choice for most cases of acute life-threatening pulmonary embolism is streptokinase." 1

1 Comparison by Controlled Clinical Trial of Streptokinase and Heparin in Treatment of Life-threatening Pulmonary Embolism. Brit. med. J. **1.** 343 (1974).

KABIKINASE

(pure streptokinase)

Full information, brochure and wall card on request.

Kabikinase is manufactured by AB Kabi, Stockholm, Sweden, and is available only from:

KabiVitrum

KabiVitrum Limited,
Bilton House,
Uxbridge Road,
London W5 2TH
Telephone: 01-567 4717 01-579 1871

P.L. No. 0022/5006
Kabikinase is a registered trade m

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU